

Fig. 1

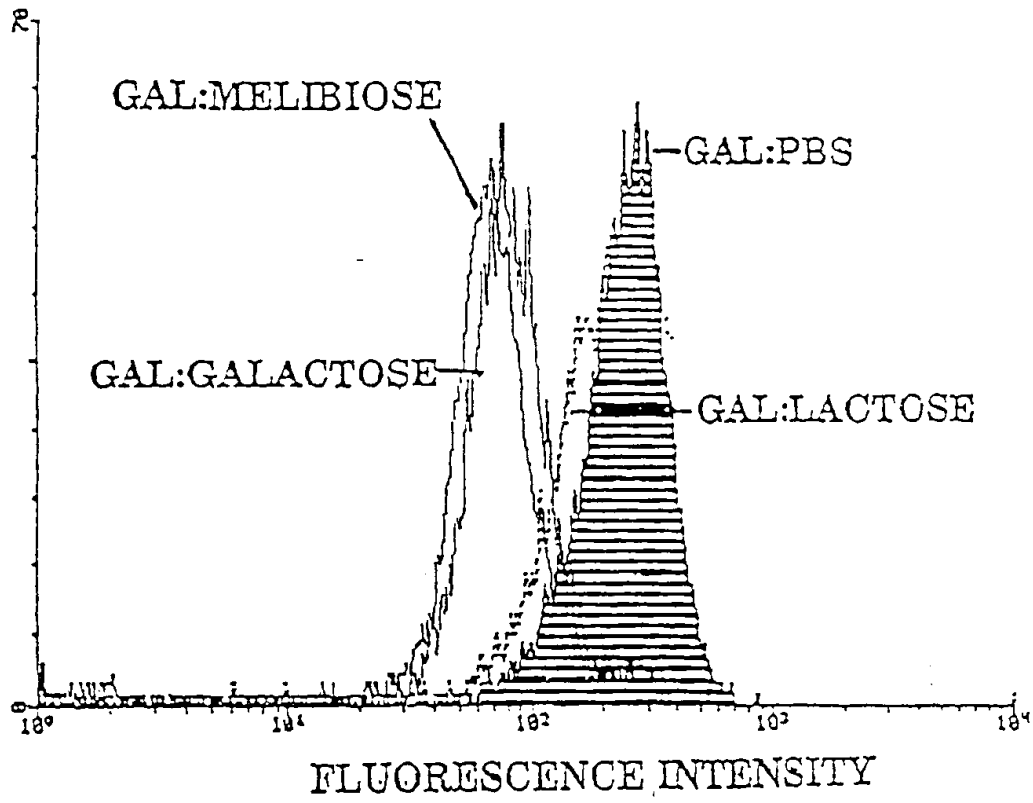


FIGURE 2

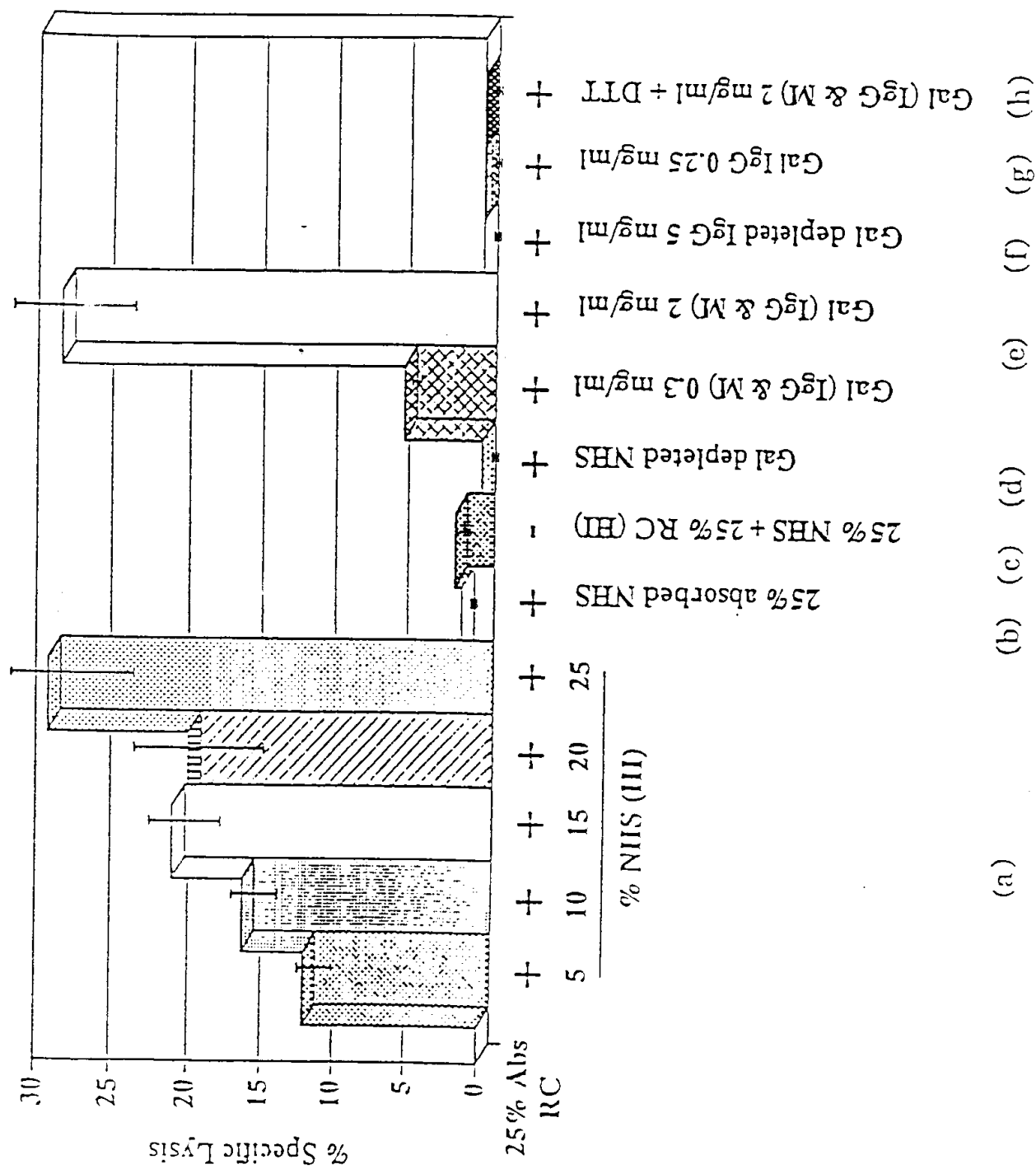
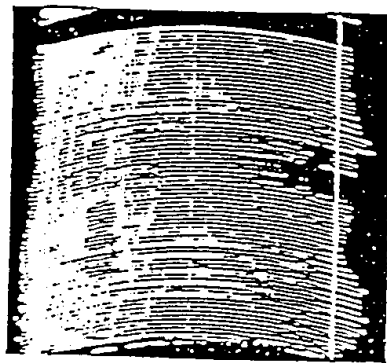


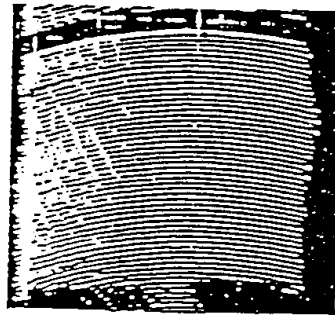
FIGURE 3



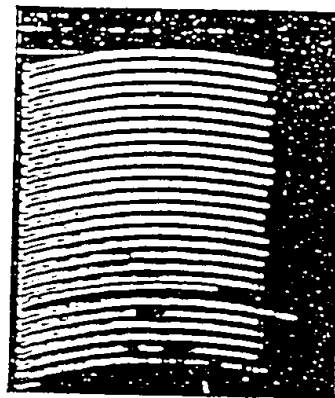
Baseline



10mM Melibiose



5 % plasma



13% plasma

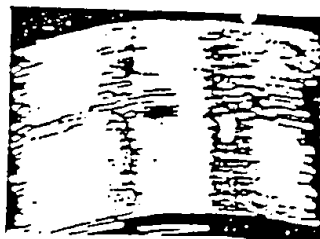


Fig 1

FOR Line-up (nt):

PCTCD	1	-----	-----	-----	-----	50
DOVGSTA	1	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	50
MUSGLYTNG	1	-----	-----	-----	-----	50
PCTCD	51	-----	-----	-----	-----	100
DOVGSTA	51	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	100
MUSGLYTNG	51	-----	-----	-----	-----	100
PCTCD	101	-----	-----	-----	-----	150
DOVGSTA	101	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	150
MUSGLYTNG	101	-----	-----	-----	-----	150
PCTCD	151	-----	-----	-----	-----	200
DOVGSTA	151	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	200
MUSGLYTNG	151	-----	-----	-----	-----	200
PCTCD	201	-----	-----	-----	-----	250
DOVGSTA	201	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	250
MUSGLYTNG	201	-----	-----	-----	-----	250
PCTCD	251	-----	-----	-----	-----	300
DOVGSTA	251	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	300
MUSGLYTNG	251	-----	-----	-----	-----	300
PCTCD	301	-----	-----	-----	-----	350
DOVGSTA	301	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	350
MUSGLYTNG	301	-----	-----	-----	-----	350
PCTCD	351	-----	-----	-----	-----	400
DOVGSTA	351	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	400
MUSGLYTNG	351	-----	-----	-----	-----	400
PCTCD	401	-----	-----	-----	-----	450
DOVGSTA	401	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	450
MUSGLYTNG	401	-----	-----	-----	-----	450
PCTCD	451	-----	-----	-----	-----	500
DOVGSTA	451	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	500
MUSGLYTNG	451	-----	-----	-----	-----	500
PCTCD	501	-----	-----	-----	-----	550
DOVGSTA	501	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	550
MUSGLYTNG	501	-----	-----	-----	-----	550
PCTCD	551	-----	-----	-----	-----	600
DOVGSTA	551	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	CGCGCGCGCG	600
MUSGLYTNG	551	-----	-----	-----	-----	600

Fig 4 (cont) 4-2

			Exon 3 ↓ Exon 4	
PGTCD	601	-----	-----	650
BOVGSTA	601	-----	-----	650
MUSGLYTNS	601	CAAGTCAGAA	ACAAGTCTTC CATCCTCAAC ATCTCGATCA CAGCAGAAA	650
		START		
PGTCD	651	TAATGAATCT	CAAGCCAAAG CTGCTTCTCT CATCTCTGCT TGTCTCAACT	700
BOVGSTA	651	TAATGAATCT	CAAGCCAAA CTGATTCTCT CAATCTCTGCT TGTCTCAACT	700
MUSGLYTNS	651	TAATGAATCT	CAAGCCAAA CTAACTCTCT TCACTCTCAT TGTCTCAACT	700
			Exon 4 ↓ Exon 5	
PGTCD	701	GTAATGCTTG	TGTTTTGGCA ATACATCAAC AGCCGACAAG GTTCTTTCTT	750
BOVGSTA	701	GTCATTGTTG	TGTTTTGGCA ATATATCCAC AGCCGACAAG GCTCTTTCTT	750
MUSGLYTNS	701	GTGCTTCTCG	TGTTTTGGCA ATATCTCAAC AGCCGACAGC GCTCTTTCTT	750
			Exon 5 ↓ Exon 6	
PGTCD	751	CTGGATATAC	CAGTCAAAA ACCCAGAACT TGGCAGCACT GGTCAAGGG	800
BOVGSTA	751	CTGCATAAAC	CCATCAAGAA ACCCAGAACT TGGTGGCAGC AGCAATCAGA	800
MUSGLYTNS	751	CTGGATATAT	CACACAAAA TTCCAGAGCT TGGTCAAGAC AGATGGCAGA	800
			Exon 6 ↓ Exon 7	
PGTCD	801	GCTGCTGG--	TTTCCGAGC TGGTTTAACTA ATGGCACTCA CAGTTACCA	850
BOVGSTA	801	AGGCTCTGTC	GCTTCCGACA TGGTTTAACTA ATG-----	850
MUSGLYTNS	801	AGCACTGGTG	GTTCCGAGC TGGTTTAAAA ATGGCACTCA CAGTTATCA	850
PGTCD	851	CAACAGCAAG	ACGCTATAGC CAACGAAAAG CAACAAACAA AACAGACAA	900
BOVGSTA	851	CAACAGCATC	CACACATAAA CGAAGAAAAG CAACAAACAA ACCAAGACCA	900
MUSGLYTNS	851	CAACAGCAAGC	TACAGGAGC CACACAAAA GGTACAAATG CAGATGGCAT	900
			Exon 7 ↓ Exon 8	
PGTCD	901	CACAGCAGAC	CTTCCGCTAG TGGACTGCTT TAATCTGAG AAACGCGCAG	950
BOVGSTA	901	---AAGCAAG	CTTAAGCTAT CGGACTGCTT CAACCCATTT AAACGCGCGC	950
MUSGLYTNS	901	---TGAAGAC	CTCAGCTAT CGGACTGCTT CAATCCAAAG AAACGCGCGC	950
PGTCD	951	AGGCTGTGAC	CATAACCAGA TGGAAAGGCTC CAGTGGTATG GGAAGGCACT	1000
BOVGSTA	951	AGGTTGTGAC	CATGACCAAC TGGAAAGGCTC CAGTGGTATG GGAAGGCACT	1000
MUSGLYTNS	951	ATGTTTTCAC	ACTGACCCCG TGGAAAGGCG CCATTGTCTG GGAAGGCACT	1000
PGTCD	1001	TACAACAGAG	CCGTCTTACA TAATTATAAT GCCAAGCACA AAATTACCGT	1050
BOVGSTA	1001	TACAACAGAG	CCGTCTTACA CAATTATTAT GCCAAGCACA AAATTACCGT	1050
MUSGLYTNS	1001	TATCAGACAG	CTCTGCTGCA AAAGTACTAC CCCACACACA AACTCACTGT	1050
			Exon 8 ↓ Exon 9	
PGTCD	1051	GGCCTTGACC	CTTTTCTGCT TGGCAAGATA CATTGAGCAT TACTTCCAGG	1100
BOVGSTA	1051	GGCCTTGACC	CTTTTCTGCT TGGCAAGATA CATTGAGCAT TACTTCCAGG	1100
MUSGLYTNS	1051	GGCCTTGACA	CTTTTCTGCT TGGCAAGATA CATTGAGCAT TACTTACAA	1100
PGTCD	1101	AGTTCTTAAT	ATCTGCAAA ACATACTTCA TGGTGGGCA CAAGTCAATC	1150
BOVGSTA	1101	AGTTCTTAAC	GTCTGCTAAT AAGCACTTCA TGGTGGGCA CCCAGTCAATC	1150
MUSGLYTNS	1101	ACTTTCTGCA	GTCTGCTGAC ATCTACTTCA TGGTGGGCA TGGGCTCAAT	1150
PGTCD	1151	TTTTACATCA	TGGTGGATCA TATCTCCAGC ATGCGTTTCA TACAGCTGGC	1200
BOVGSTA	1151	TTTTATATCA	TGGTGGATCA TGTCTCCAGC ATGCGTTTCA TACAGTGGC	1200
MUSGLYTNS	1151	TTTTACGTCA	TCATAGATCA CACCTCCCGC ATGCGTCTG TGCACCTGAA	1200
PGTCD	1201	TGCTCTGGCC	TGCTTTAAAG TGTTTGACAT CAAGTCCGAC AAGAGCTGGC	1250
BOVGSTA	1201	TGCTCTGGCC	TGCTTTAAAG TGTTTAAGAT CAAGCTCGAC AAGAGCTGGC	1250
MUSGLYTNS	1201	CCCTCTACAT	TGCTTTAAAG TGTTTGACAT CAGCTCTGAC AAGAGCTGGC	1250

PCTCD	1251 AACACATCAG CATGATCCGC ATGAAGACCA TCGGGGACCA CATCGTGGCC	1300
BOVGSTA	1251 AGGACATCAG CATGATCCGC ATGAAGACTA TCGGGGACCA CATCGTGGCC	1300
MUSGLYTN	1251 AGGATATCAG CATGATCCGC ATGAAGACCA TTGGGGACCA CATCGTGGCC	1300
PCTCD	1301 CACATCCAGC ACCAGCTTCA CTTCCTCTTC TGCATCCAGC TGCATCAGGT	1350
BOVGSTA	1301 CACATCCAGC ATGAGCTTCA CTTCCTCTTC TGCATCCAGC TGCATCAGGT	1350
MUSGLYTN	1301 CACATCCAGC ACCAGCTTCA CTTCCTCTTC TGCATCCAGC TGCATCAGGT	1350
PCTCD	1351 CTTCGAAAAC AACTTTGGCC TCGAGACCTT GGGCCAGTCC GTCCCTCAGC	1400
BOVGSTA	1351 CTTCGAAAC AACTTTGGCC TCGAGACCTT GGGCCAGTCC GTCCCTCAGC	1400
MUSGLYTN	1351 CTTCGAAAC AACTTTGGCC TCGAAACTCT GGGCCAGCTC CTACCCAGCC	1400
PCTCD	1401 TACAGGCCCTG GTGGTACAAAG GCAGATCCCTG ACCAGTTTAC CTACCCAGCC	1450
BOVGSTA	1401 TACAGGCCCTG GTGGTACAAAG GCAGATCCCA ATGACTTTCAC CTACCCAGCC	1450
MUSGLYTN	1401 TCGAGGCCCTG GTGGTACAAAG GCGAGTCCCG AGAAGTTTAC CTATGAGAGG	1450
PCTCD	1451 CGGAAAGCAGT CGGCAAGCTA CATTCGGTTT CGGCAAGGCG ATTTTATTA	1500
BOVGSTA	1451 CGGAAAGCAGT CTGCAAGCTA CATTCGGTTT CGGCAAGGCG ATTTTATTA	1500
MUSGLYTN	1451 CGGAAACTCT CGGCGGCTA CATTCGATTC CGCAAGGCGG ATTTTACTA	1500
PCTCD	1501 CCACCCAGCC ATTTTGGGG GAACACCCAC TCAGGTTCTA AACATCAGTC	1550
BOVGSTA	1501 CCATGCAAGCC ATTTTGGGG GAACACCCAC TCAGGTCCTT AACATCAGCC	1550
MUSGLYTN	1501 CCACCCGGCC ATTTTGGGAC GAACCCCTAC TCACATTCTC AACCTCAGCA	1550
PCTCD	1551 AGGAGTGCTT CAAGGGAATC CTCAGGACA AGGAAATGA CATAGAAGCC	1600
BOVGSTA	1551 AGGATGCTT CAAGGGAATC CTCAGGACA AGAATAATGA CATAGAAGCC	1600
MUSGLYTN	1551 CGGAGTGCTT TAAGGGGATC CTCAGGACA AGAAACATGA CATAGAAGCC	1600
PCTCD	1601 CACTGCCATC ATGAAGCCA TCTAAACAA TATTAAATTC TCACAAAGCC	1650
BOVGSTA	1601 CAATGCCATC ATGAAGCCA TCTAAACAA TATTTCCTTC TCACAAAGCC	1650
MUSGLYTN	1601 CACTGCCATC ATCAGACCCA CCTCAACAA TACTTCCTTT TCACAAAGCC	1650
PCTCD	1651 CACTAAATC TTATCCCCAG AATAGTCTG GCATTATCAT ATAGCCATGT	1700
BOVGSTA	1651 TACTAAATC TTATCCCCGG AATAGTCTG GCATTATCAC ATAGCCCTAG	1700
MUSGLYTN	1651 CACTAAATC CTATCTCCAG AGTATTCTG GCACTATCAG ATAGCCCTCC	1700
PCTCD	1701 CTCTCCATAT TACCATGTC AACATAGCTT GCCAGAAAA AGACTATAAT	1750
BOVGSTA	1701 CTCCGCATAT TAACTTCTC AACATGCTT GCCAGACAAA AGACTATAAT	1750
MUSGLYTN	1701 CTTACATAT TAAAGTCTC AACATAGCTT GCCAGACAAA AGACTATAAT	1750
PCTCD	1751 TTGGTTAGAA ATAACATCTG ACTTTAAATT GTGCCAGCAG TTTTCTCAAT	1800
BOVGSTA	1751 TTGGTTAGAA ATAATCTCTG ACTT-----T GTGCCAGTAC ATTTCTCAAT	1800
MUSGLYTN	1751 TTGGTTAGAA ATAATCTCTG ACTTCAAAAT GTG----- --ATGGAAC	1800
PCTCD	1801 TTCAAAAGCT ATTACTCTGG CTACTTCTC ACAGAAAGTAG ---CACTTAA	1850
BOVGSTA	1801 TTGAGAGCT ATTATTCTGG CTACTTCTC ACAAAAGTAA ---CACTTAA	1850
MUSGLYTN	1801 TTCAAC--T ATTACTCTGG CTAAATCTC AAACAAGTAG CAACACTTCA	1850

stop

Fig. 4(cont) 4 - 4

POTCD	1051	TTTTAACTTT	TAATAAATA	CTAACAAA-	----TACCAA	CACAGTAA-G	1900
BOVGSTA	1051	TTTTAACTTA	AAAAAATA	CTAACAAA-	----GACCAA	CACAGCAA-A	1900
MUSGLYTN	1051	TTTCAACTTT	TAAGAAG-A	CAATCAAAAC	CAAAACCCAC	TACCATGGCA	1900
POTCD	1901	TACATATTAT	TCTTCTTTC	AACCTTGAGC	CTTGTCAAA	GGCAGAAATCA	1950
BOVGSTA	1901	TACATATTAT	TCTTCTTTC	AACCTTGAGC	CTTGTAAATAC	GGCAGAAATCA	1950
MUSGLYTN	1901	AACAGATCAT	TCTTCTT-CA	CACCTTGAGC	CT-GTAAAT	GTACAGAAAC	1950
POTCD	1951	CTCTGTGC--	--TAATCAGA	TGTAAATTCC	CAGTCAATTC	.....	2000
BOVGSTA	1951	ACCTGTGC--	--TAATCAGA	TGTAAATTCC	CAGTCAATTC	TTACCTAATTC	2000
MUSGLYTN	1951	CTCTATGGCA	AGTAATCAGG	TATAAATTCT	CAATCAATTC	TTACATATTC	2000
POTCD	2001	.....	.....	.....	.....	.....	2050
BOVGSTA	2001	TTCTTCTCTG	GGCGGGGGA	TGGATACACC	ATCAATTTGA	CC.....	2050
MUSGLYTN	2001	TGCTCTTCTG	GAAGAGTCA	TTCTACAAAT	CAAAATTAAT	TTACAGAAAC	2050
POTCD	2051	.....	.....	.....	.....	.....	2100
BOVGSTA	2051	.....	.....	.....	.....	.....	2100
MUSGLYTN	2051	AAAGACAT	GGCGGAAC	TCTTCTCAGT	CTGTCAATCA	ATTCAACCAT	2100
POTCD	2101	.....	.....	.....	.....	.....	2150
BOVGSTA	2101	.....	.....	.....	.....	.....	2150
MUSGLYTN	2101	GGCAGCTGC	TCAGAGAAC	ATTAGGGAAC	AGTGTCTCTT	GTGTCAAGCT	2150
POTCD	2151	.....	.....	.....	.....	.....	2200
BOVGSTA	2151	.....	.....	.....	.....	.....	2200
MUSGLYTN	2151	TGCAGGCTC	CATCTCTTT	GCTTCATTA	CTTCTCTCTC	ATGGAGATTC	2200
POTCD	2201	.....	.....	.....	.....	.....	2250
BOVGSTA	2201	.....	.....	.....	.....	.....	2250
MUSGLYTN	2201	TAAAGCAAC	CACAGAGCT	TTGCAGGAC	ACACCTTTAA	TAAAGATTC	2250
POTCD	2251	.....	.....	.....	.....	.....	2300
BOVGSTA	2251	.....	.....	.....	.....	.....	2300
MUSGLYTN	2251	AATGTCAAC	TCAGTCTTA	AAAGTCAAT	GCTTCAGGAC	CGCTGGCAGT	2300
POTCD	2301	.....	.....	.....	.....	.....	2350
BOVGSTA	2301	.....	.....	.....	.....	.....	2350
MUSGLYTN	2301	CCAGGCGCCA	CTAGCTAAT	GTCTCTCTCC	TGCGCATAA	GCAGGAGAC	2350
POTCD	2351	.....	.....	.....	.....	.....	2400
BOVGSTA	2351	.....	.....	.....	.....	.....	2400
MUSGLYTN	2351	AGTGGCAAT	GCTACTTTC	TGCGCATAT	TCAGATTC	GGAAATTA	2400
POTCD	2401	.....	.....	.....	.....	.....	2450
BOVGSTA	2401	.....	.....	.....	.....	.....	2450
MUSGLYTN	2401	AGCGTCAAC	CTTACAGGA	CATAGCACT	GCGTCTGCT	ATTCAATCA	2450
POTCD	2451	.....	.....	.....	.....	.....	2500
BOVGSTA	2451	.....	.....	.....	.....	.....	2500
MUSGLYTN	2451	GTACAAACA	CACAGAGTT	TCTTCAAGAT	GACTAACAG	AGCAATTA	2500

Fig. 4(cont.) 4-5

PGTCD	2501	.....	.....	.....	.....	2550	
BOVGSTA	2501	.....	.....	.....	.....	2550	
MUSGLYTHS	2501	TGCAAACTGT	CTTCATTTTC	TTTTGGCCAA	ATTGTATTCA	TGCTGTAAOC	2550
PGTCD	2551	.....	.....	.....	.....	2600	
BOVGSTA	2551	.....	.....	.....	.....	2600	
MUSGLYTHS	2551	TTTGTGTGTT	CAGCCCTGTC	CAGAGGGTGT	CAGTGTATCA	GGGAGGACA	2600
PGTCD	2601	.....	.....	.....	.....	2650	
BOVGSTA	2601	.....	.....	.....	.....	2650	
MUSGLYTHS	2601	CTACCTCAGC	CGACTCAGCA	CGAGCAGCCT	ATTATATCAG	AACACAACT	2650
PGTCD	2651	.....	.....	.....	.....	2700	
BOVGSTA	2651	.....	.....	.....	.....	2700	
MUSGLYTHS	2651	CTCATCATCA	CGTCCCTACCT	ACAACCTGCT	CTGAACTGCC	CAGTTCCTCA	2700
PGTCD	2701	.....	.....	.....	.....	2750	
BOVGSTA	2701	.....	.....	.....	.....	2750	
MUSGLYTHS	2701	CGCCATCCTC	TTCCAGTCTG	CGCCCTCTTA	TGCAGCAGCT	CAGTCAAGAC	2750
PGTCD	2751	.....	.....	.....	.....	2800	
BOVGSTA	2751	.....	.....	.....	.....	2800	
MUSGLYTHS	2751	AAAGCCCCCT	CTCACATGAC	CTCATTTCCC	CTGCTCTAGT	ACTATGCAAG	2800
PGTCD	2801	.....	.....	.....	.....	2850	
BOVGSTA	2801	.....	.....	.....	.....	2850	
MUSGLYTHS	2801	TGTGACAGCC	AGCCAGCCAG	ATGTACTGCA	CAACATAGCA	AGCCACTTCA	2850
PGTCD	2851	.....	.....	.....	.....	2900	
BOVGSTA	2851	.....	.....	.....	.....	2900	
MUSGLYTHS	2851	TGGCATGCG	AGCCGCACTC	ACTACAACCC	AGCTGCTCAA	CGTTCTGTTC	2900
PGTCD	2901	.....	.....	.....	.....	2950	
BOVGSTA	2901	.....	.....	.....	.....	2950	
MUSGLYTHS	2901	CGCCCTCTCA	CAGCCTGCAG	CAGCCCTGTT	ATAGCTGGTT	CTCAAGCTAT	2950
PGTCD	2951	.....	.....	.....	.....	3000	
BOVGSTA	2951	.....	.....	.....	.....	3000	
MUSGLYTHS	2951	GGCTGCGCAC	CGCTTTGGCA	AGTGTAAAT	CAGCCTTTCA	CAGCTGTCCC	3000
PGTCD	3001	.....	.....	.....	.....	3050	
BOVGSTA	3001	.....	.....	.....	.....	3050	
MUSGLYTHS	3001	CTAACAGCCT	TAAAAACAT	AGATATTTCC	ACTCTGACTC	GTAAAGTAG	3050
PGTCD	3051	.....	.....	.....	.....	3100	
BOVGSTA	3051	.....	.....	.....	.....	3100	
MUSGLYTHS	3051	CAGAAATACA	GTATGAAAT	AGCAAGCGAA	ATAATTCTCC	CGTTCTGTTC	3100



Fig 5

PBM Line-up (aa):

		Ex4 ↓ Ex5	Ex5 ↓ Ex6	
PCT(Frame 1)	1	MNVKGRVVL	MLVSTVMV	PHEYNISPEC SLFWIYQSKN PEVCG-SSAQR 50
BGT(Frame 1)	1	MNVKCKVIL	MLVSTVIW	PHEYNISPEC SLFWINPSRN PEVCGSSIQK 50
MGT(Frame 1)	1	MNVKCKVILL	MLIVSTVVV	PHEYNISPDG SPLWIIYHTKI PEVGENRWQK 50
		Ex6 ↓ Ex7	Ex7 ↓ Ex8	
PCT(Frame 1)	51	GMWFPSWFNN	GTHSYNEEDD	AIGNEXZQRK EDRGSELPLV DWFNPEKRPE 100
BGT(Frame 1)	51	GMWLPWFNN	G---YKEEDG	DINEEKQGRN ED-ECXKLS DWFNPTKRPE 100
MGT(Frame 1)	51	DWHPFSPFKH	GTHGYQEDIV	EGRRK-GRN GDRIEEPQLW DWFNPKNRPD 100
		Ex8 ↓ Ex9		
PCT(Frame 1)	101	AVTITRWKAP	VWECTYNRA	VLDNYHAKQK ITVGLTVFAV GRYTEHYLEZ 150
BGT(Frame 1)	101	VVTHTRWKAP	VWECTYNRA	VLDNYHAKQK ITVGLTVFAV GRYTEHYLEZ 150
MGT(Frame 1)	101	VLTVTPWKAP	IVWECTYDTA	LLEKYYATCK LTVGLTVFAV GRYTEHYLED 150
PCT(Frame 1)	151	FLISANTYFM	VGHXYIFYM	VDDISRMPLI ELQPLASFKV FEIKSEKRWQ 200
BGT(Frame 1)	151	FLTSANKIHM	VGHPIVIFYM	VDDVERMPLI ELQPLASFKV FEIKSEKRWQ 200
MGT(Frame 1)	151	FLESAENYFM	VGHVIFYM	IDDTSRMPLV KLNPLHSIQV FEIRSEKRWQ 200
PCT(Frame 1)	201	DISHMRKTI	GEHILAHIQH	EVDFLFCMDV DQVFQNNFGV ETLOQSSVAQL 250
BGT(Frame 1)	201	DISHMRKTI	GEHIVAHIQH	EVDFLFCMDV DQVFQDKFGV ETLGZSVAQL 250
MGT(Frame 1)	201	DISHMRKTI	GEHILAHIQH	EVDFLFCMDV DQVFQDNFGV ETLOQLVAQL 250
PCT(Frame 1)	251	QANWYKAPD	EFTYERRKES	AAIYPFGCGD FYYHAAIFGG TPTQVLNITQ 300
BGT(Frame 1)	251	QANWYKADPH	DFTYERRKES	AAIYPFGCGD FYYHAAIFGG TPTQVLNITQ 300
MGT(Frame 1)	251	QANWYKASPE	KFTYERRELS	AAIYPFGCGD FYYHAAIFGG TPTHILNLTR 300
PCT(Frame 1)	301	ECFKGILQOK	ENDIEAQWHD	ESHLNKYLIL NKPTKILSPE YCHDYHIGMS 350
BGT(Frame 1)	301	ECFKOILKOK	KNDIEAQWHD	ESHLNKYFLL NKPTKILSPE YCHDYHIGLP 350
MGT(Frame 1)	301	ECFKGILQOK	KNDIEAQWHD	ESHLNKYFLP NKPTKILSPE YCHDYQIGLP 350
PCT(Frame 1)	351	VDIRIVKIAN	QKKEYNLVRN	NI*..... 400
BGT(Frame 1)	351	ADIKLVQMSH	QKKEYNLVRN	NV*..... 400
MGT(Frame 1)	351	SDIKSVKVAH	QKKEYNLVRN	NV*..... 400

Fig. 6.

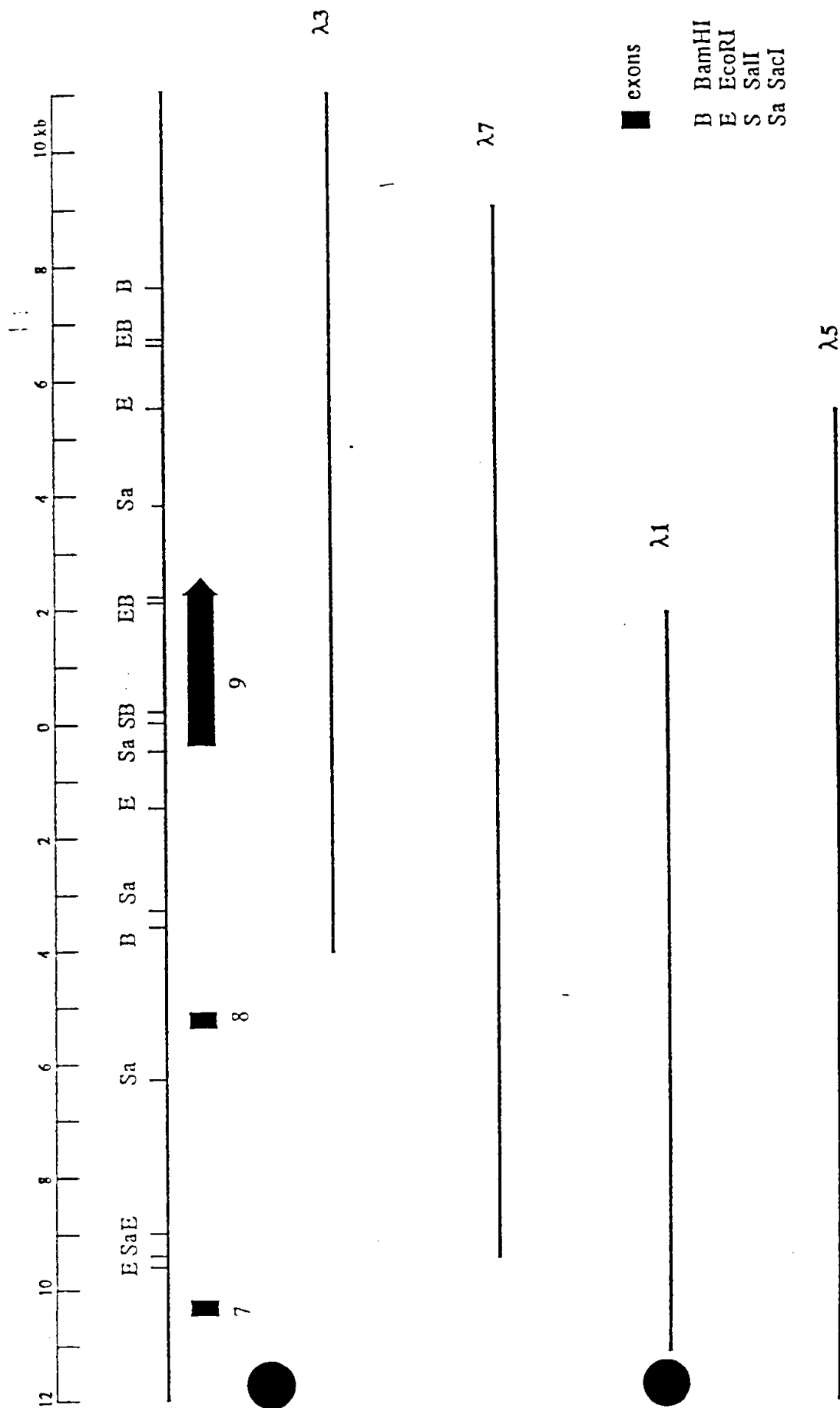
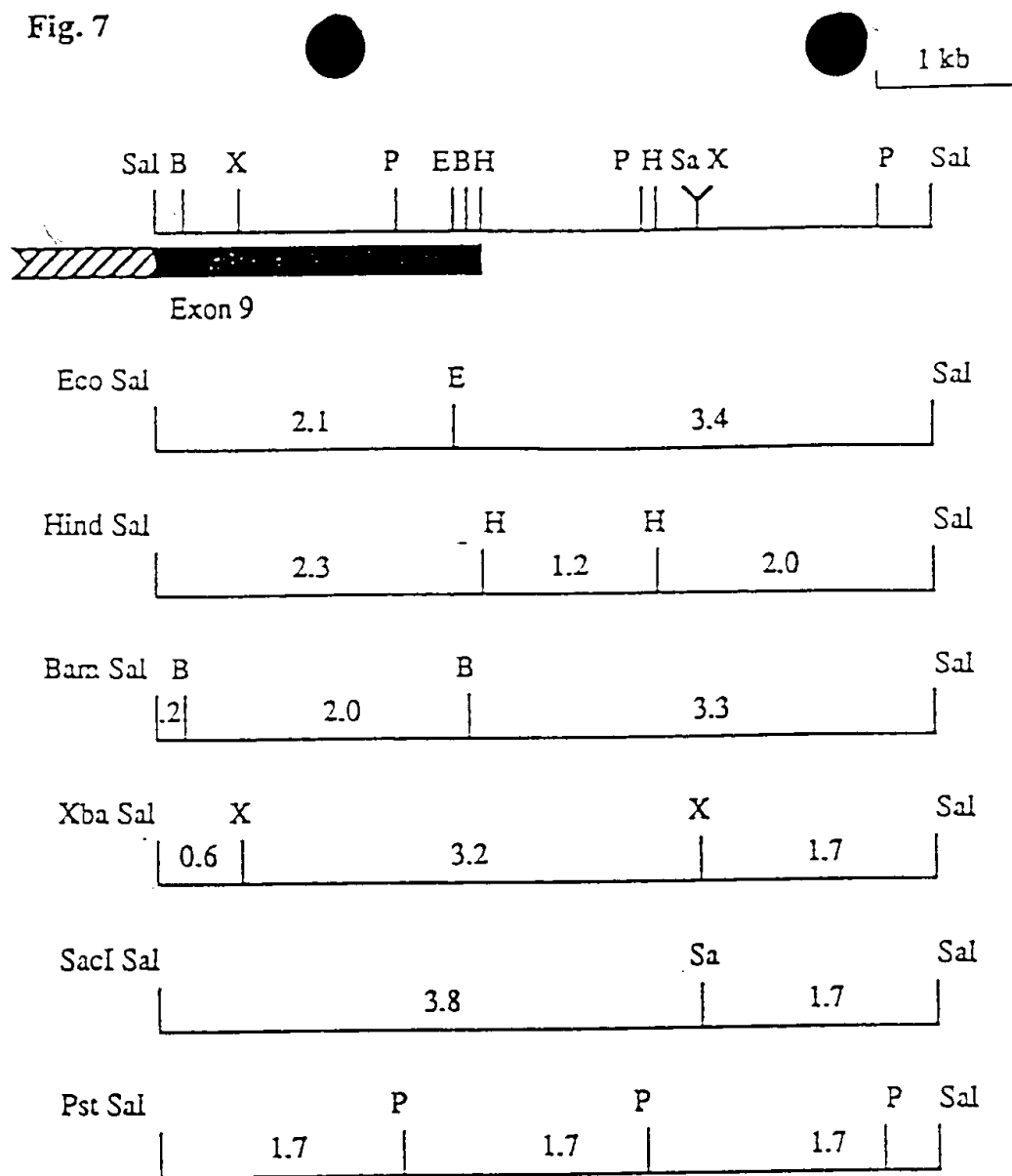


Fig. 7

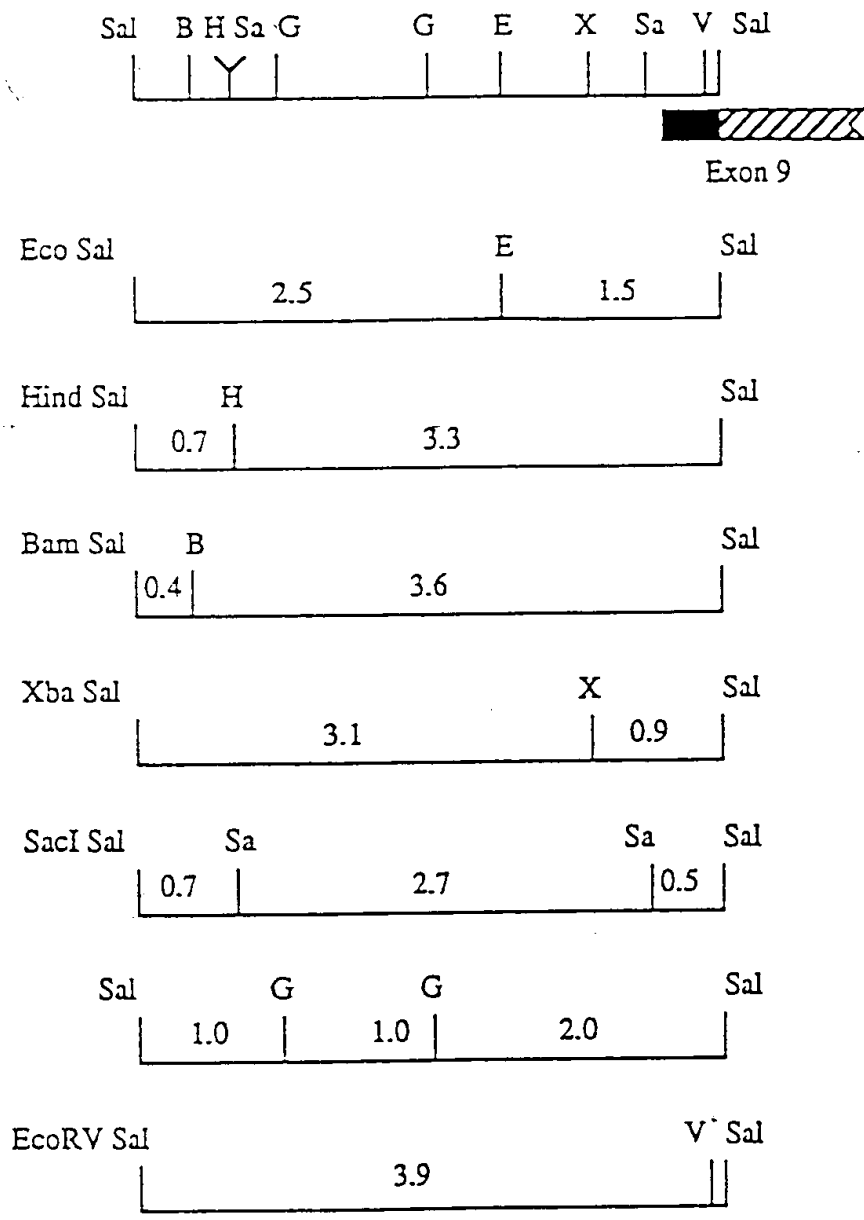


No sites for: BglII, Nde, PvuI, Xho, Kpn, SacII, EcoRV, Sma, Cla, Apa, Not

pBS+KS:

.... SacI SacII Not Xba Spe Bam Sma Pst Eco RV Hind Cla Sal Xho Apa Kpn ....





A ApaI  
B BamHI  
C ClaI  
E EcoRI  
G BglII  
H HindIII  
K KpnI  
N NotI  
P PstI  
S Sal  
Sa SacI  
V EcoRV  
X XbaI  
Xh XhoI

No sites for: Nde, PvuI, Xho, Kpn, SacII, Sma, Cla, Apa, Not

Unmapped sites for: Pst, PvuII

pUBS:

.... SacI SacII Not Xba Spe Bam Sma Pst Eco RV Hind Cla Sal Xho Apa Kpn ....



Fig. 9

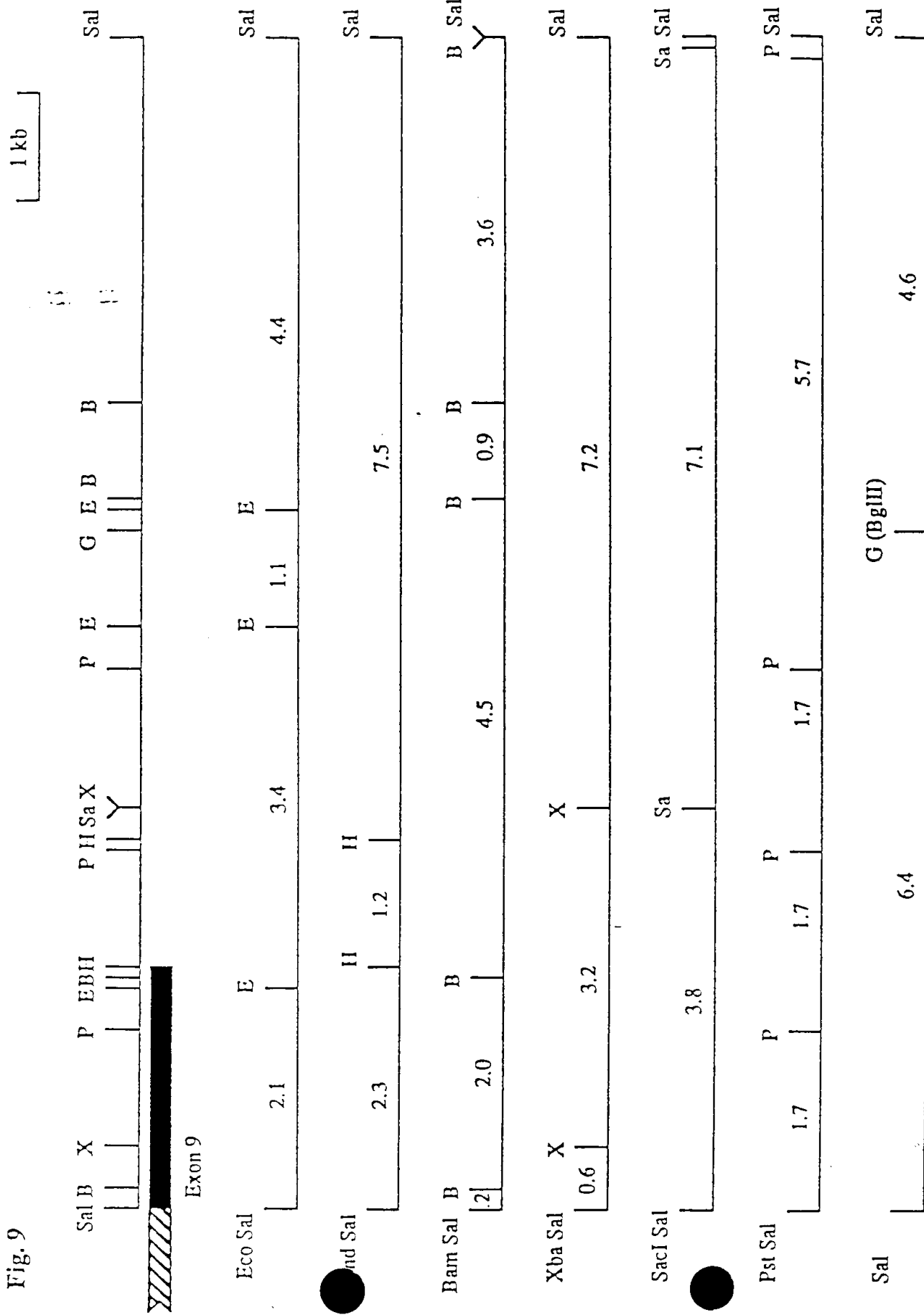


Fig. 9 (cont)

No sites for: Xho, Kpn, SacII, Sma, Cla, EcoRV, Apa, Not, PvuI, Nde

pUBS:

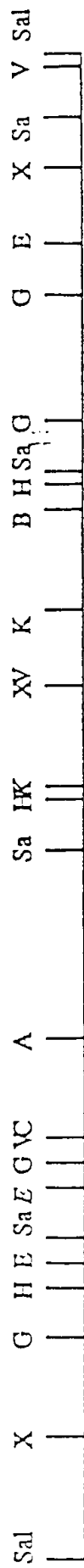
.... SacI SacII Not Xba Spe Bam Sma Pst Eco RV Hind Cla Sal Xho Apa Kpn ....



A	Apal
B	BamHI
C	ClaI
E	EcoRI
G	BglII
H	HindIII
K	KpnI
N	NotI
P	PstI
S	SalI
Sa	SacI
V	EcoRV
X	XbaI
Xh	XhoI

Fig. 10

1 kb



Exon 9

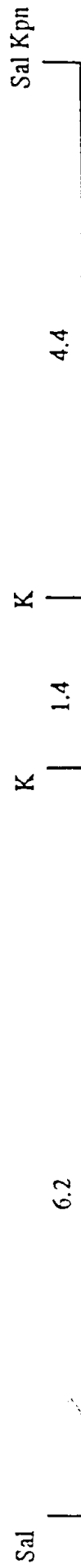
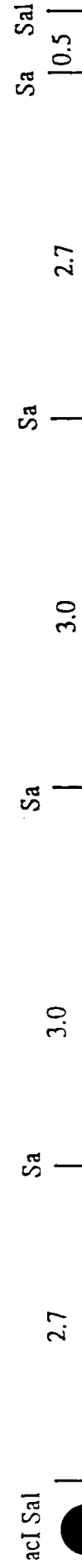
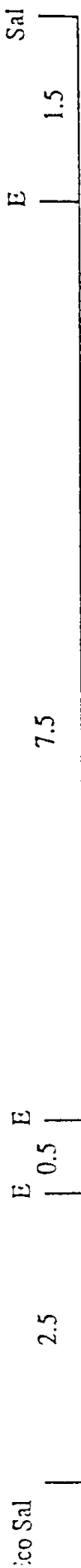
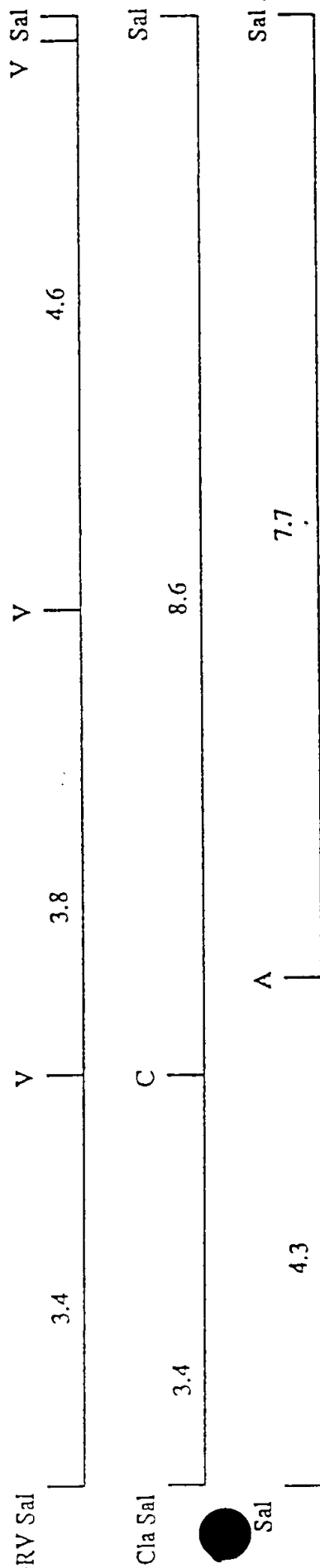


Fig. 10 (cont)



No sites for: Xho, SacII, Sma, Not

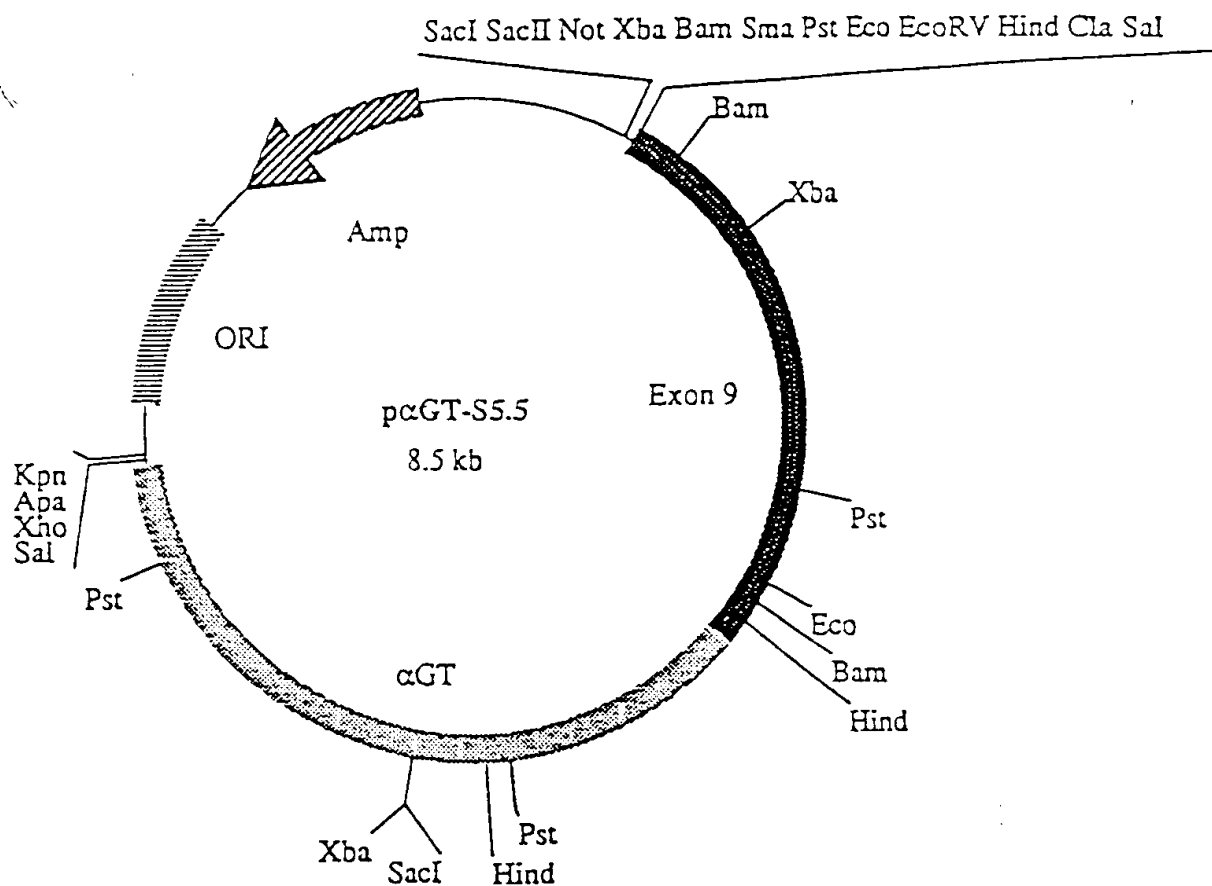
pUBS:






.... SacI SacII Not Xba Spe Bam Sma Pst Eco RV Hind Cla Sal Xho Apa Kpn ....

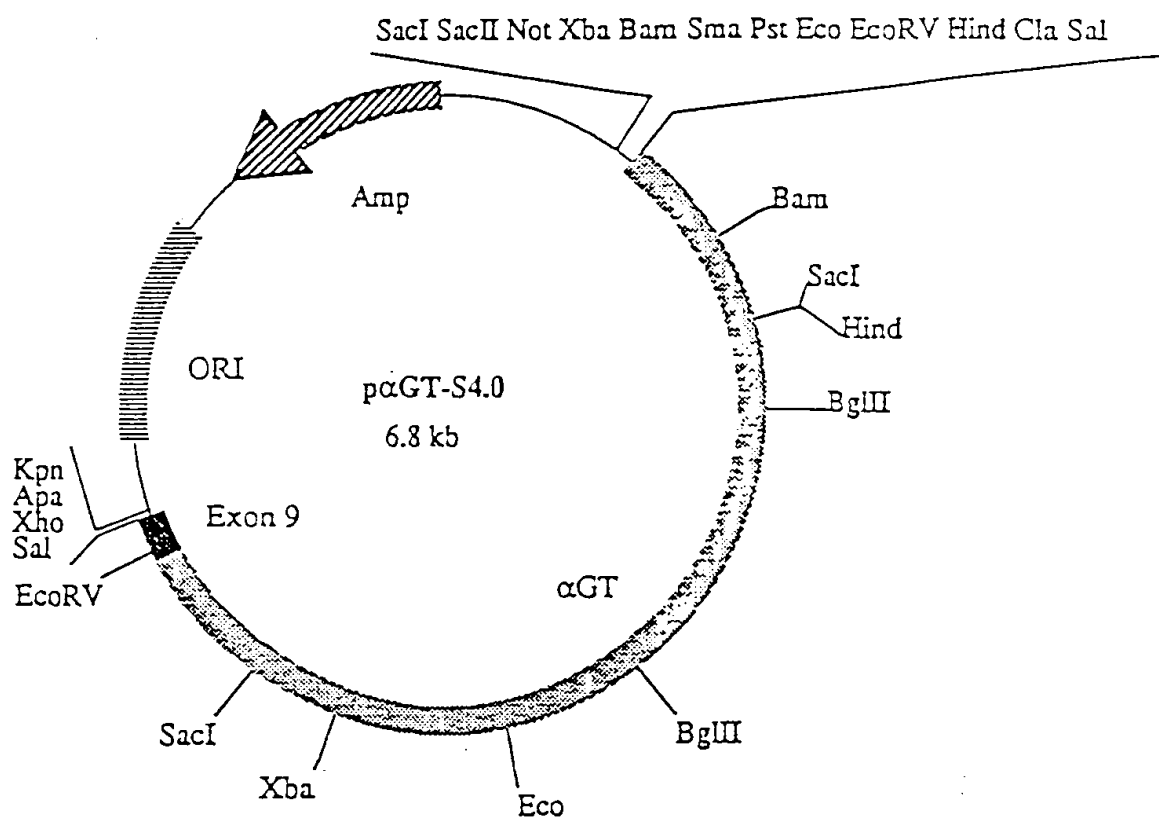







A ApaI  
B BamHI  
C ClaI  
E EcoRI  
G BglII  
H HindIII  
K KpnI  
N NotI  
P PstI  
S Sal  
Sa SacI  
V EcoRV  
X XbaI  
Xh XhoI



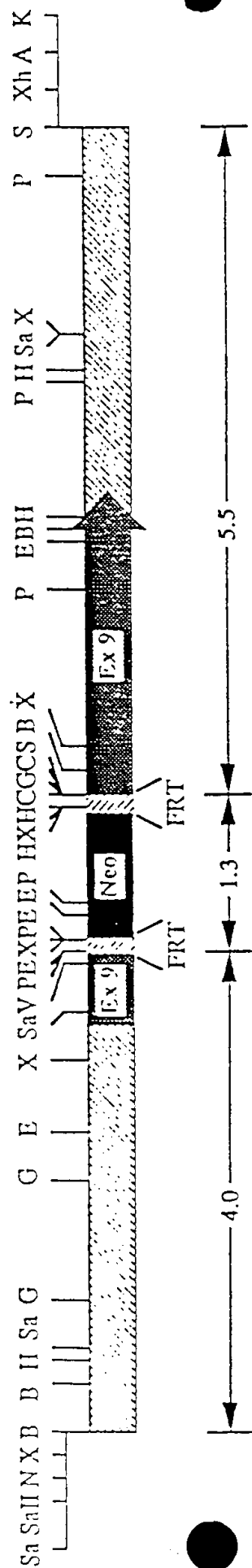


-  α1,3 galactotransferase (αGT) non-coding DNA
-  Exon 9 of αGT
-  Neo resistance gene
-  Bacterial origin of replication
-  Amp resistance gene

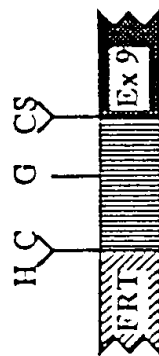









-  α1,3 galactotransferase (αGT)
-  Exon 9 of αGT
-  Neo resistance gene
-  Bacterial origin of replication
-  Amp resistance gene

ig. 13



region around Cla-Bgl linker



-   $\alpha$ 1,3 galactotransferase ( $\alpha$ GT)
-  non-coding DNA
-  Exon 9 of  $\alpha$ GT
-  Neo resistance gene
-  FRT recombination site
-  Cla-Bgl linker
-  Stop codons

- A ApaI
- B BamHI
- ClaI
- EcoRI
- G BglII
- H HindIII
- K KpnI
- N NotI
- P PstI
- S SalI
- Sa SacI
- V EcoRV
- X XbaI
- Xh XhoI

Fig. 14

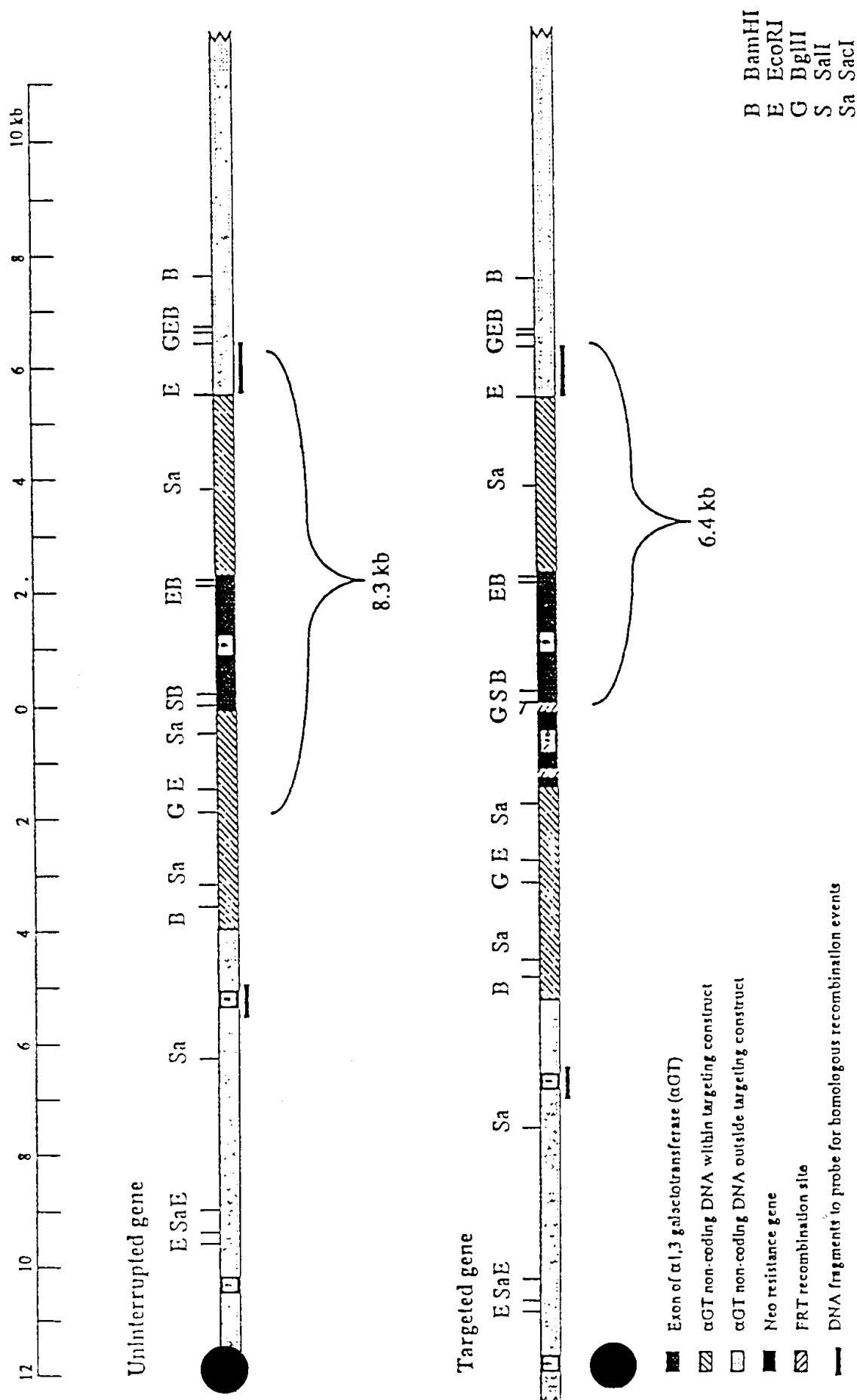
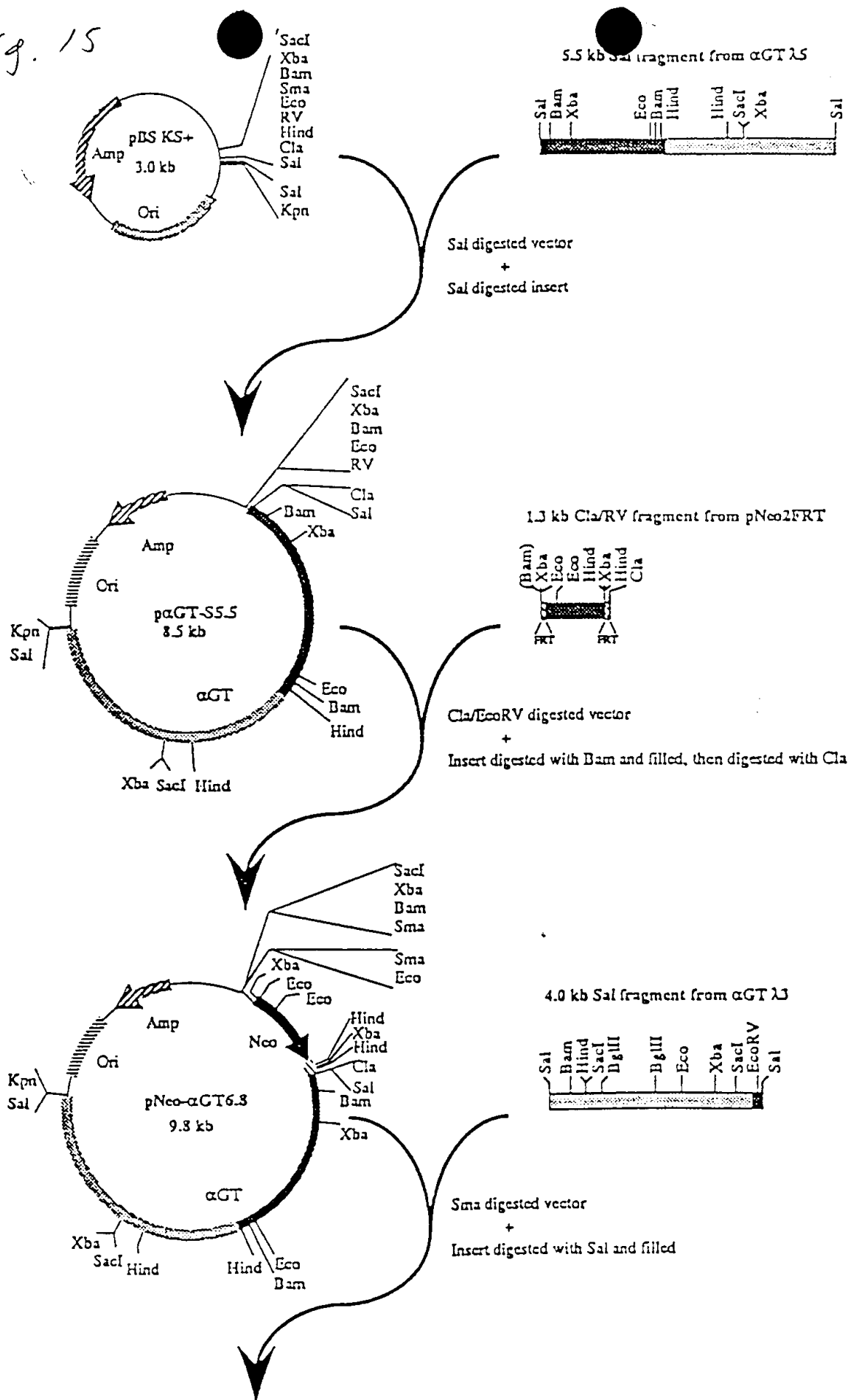
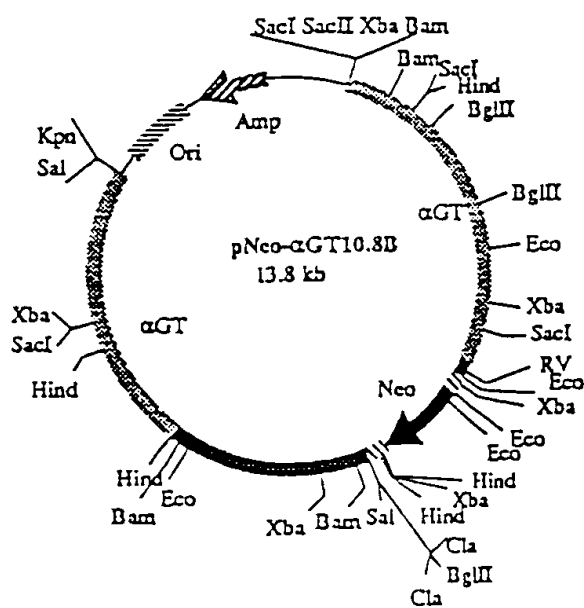
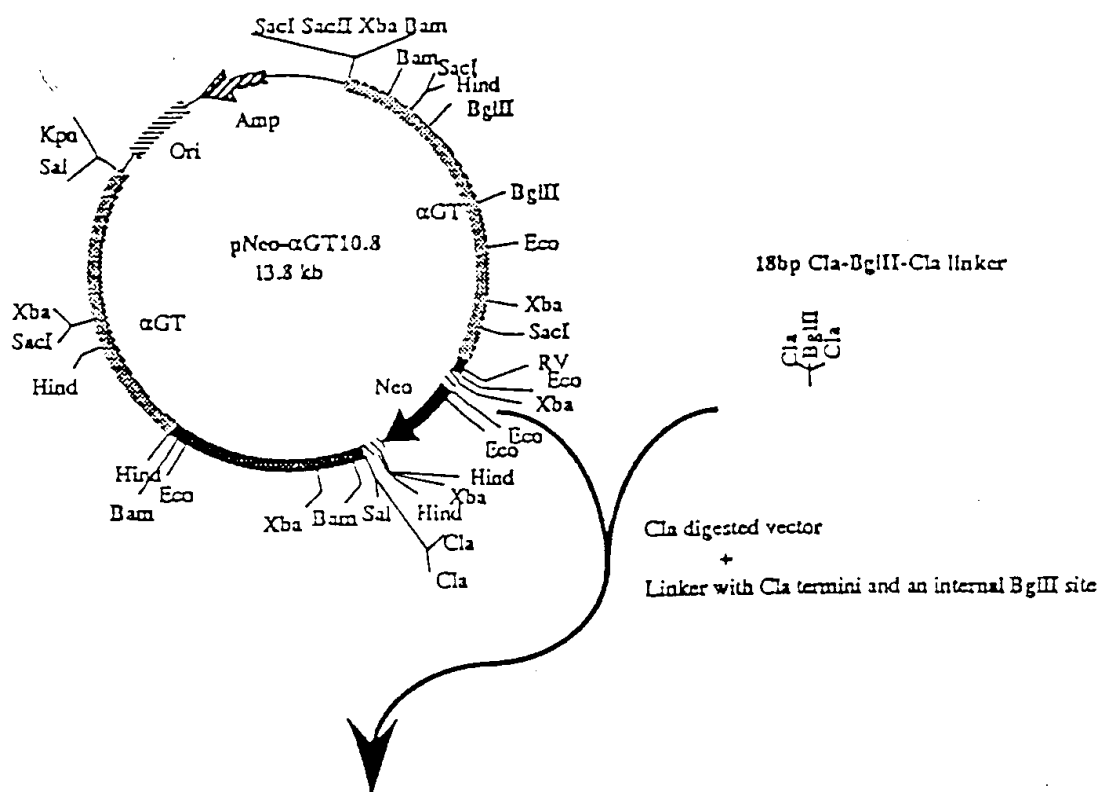


Fig. 15





- α1,3 galactotransferase (αGT) non-coding
- Exon 9 of αGT
- Neo resistance gene
- FRT recombination site
- Bacterial origin of replication
- Amp resistance gene

Fig. 16

10	20	30	40	50	60
GAGGGCTGCA	GGAAATTCGAT	GATGCCCCAG	CTTGAAGTTC	GTATTCCGAA	GTTGCTATTC
70	80	90	100	110	120
TCTAGAAAGT	ATAGGAACTT	CAAGCTGGGC	TGCAGGAATT	CGATTCCGAGC	AGTGTGCTTT
130	140	150	160	170	180
TGCAAGAGGA	AGCAAAAAGC	CTCTCCACCC	AGGCTTGGAA	TGTTTCCACC	CAATGTTCAG
190	200	210	220	230	240
CAGTGTGCTT	TTGCAAGAGG	AAGCAAAAAG	CCTCTCCACC	CAGGCTTGGAA	ATGTTTCCAC
250	260	270	280	290	300
CCAATGTGCA	GCAAACTCCG	CCCAGCTCT	TGTCATTGGC	GAATTCCGAA	ACCCAGATCC
310	320	330	340	350	360
AGTGGGGGGG	GGGGGGTCCC	AGGTCCACTT	GGCATATTAA	GGTGACGGCT	GTGGGCTGGA
370	380	390	400	410	420
ACACCGAGCG	ACCTTGCAGC	CAATATGGGA	TGGGGCATTC	AACAAGATGG	ATTGCCAGCA
430	440	450	460	470	480
GGTTCTCCGG	CCGCTTGGGT	GGAGAGGCTA	TTCCGGTATG	ACTGGGCACA	ACAGACAATC
490	500	510	520	530	540
GGCTGCTCTG	ATGCGCGCGT	GTTCCGGGCTG	TCAGCGCAGG	GGCGCCCGGT	TCTTTTGTTC
550	560	570	580	590	600
AAGACCGACC	TGTCCGGTGC	CCTGAATGAA	CTCCAAGAGC	AGGCAGCGCG	GCTATCTGTG
610	620	630	640	650	660
CTGGCCACGA	CGGGCGTTCC	TTGGCCAGCT	GTGCTCGAGC	TTGTCACTGA	AGCGGGAAGG
670	680	690	700	710	720
GACTGGCTGC	TATTGGGCGA	AGTGGCGGGG	CAGGATCTCC	TGTCACTGCA	CCTTGTCTCT
730	740	750	760	770	780
GCCGAGAAAG	TATCCATCAT	GGCTGATGCA	ATGCGGGCGG	TGCATACGCT	TGATCCGGCT
790	800	810	820	830	840
ACCTGCCCCAT	TCGACCACCA	AGCGAAACAT	CGCATCGAGC	GAGCACGTAC	TCCGATGGAA
850	860	870	880	890	900
GCCGGTCTTG	TCGATCAGGA	TGATCTGGAC	GAAGAGCATC	AGGGGCTGGC	GCCAGCCGAA
910	920	930	940	950	960
CTGTTCGCCA	GGCTCAAGGC	GCGGATGCCC	GACGGCGAGG	ATCTCGTCTG	GACCCATGGC
970	980	990	1000	1010	1020
GATGCCCTGCT	TGCCGAATAT	CATGGTGGAA	AATGGCGCGT	TTTCTGGATT	CATCGACTGT
1030	1040	1050	1060	1070	1080
GCCCCGCTGG	GTGTGGCGGA	CCGCTATCAG	GACATAGCGT	TGGCTACCGG	TGATATTGCT
1090	1100	1110	1120	1130	1140
GAAGAGCTTG	GCGGCGAATG	GGCTGACCGC	TTCTCTGTGC	TTTACGGTAT	GCGCGCTCCC
1150	1160	1170	1180	1190	1200
GATTCCGAGC	GCATCGGCTT	CTATCGGCTT	CTTGACGAGT	TCTTCTGAGG	GGATCGGCAA
1210	1220	1230	1240	1250	1260
TAAAAAGACA	GAATAAAAGC	CACGGGTGTT	GGCGGTTTGT	TCCGATCATC	AAGCTTGAAG

Fig. 16 (cont.)

1270	1280	1290	1300	1310	1320
TTCCTATTCC	GAAGTTCCTA	TTCTCTAGAA	AGTATAGGAA	CTTCAAGCTT	ATCGATGAGT
1330	1340	1350	1360	1370	1380
AGATCTTGAT	CGATACCGTC	.....	.....	.....	.....

Linker sequences : 0-28

FRT : 29-104

Polyoma virus enhancer repeats : 105-249

Herpes Simplex Virus Tyrosine Kinase promoter : 250-385

Neomycin phosphotransferase coding region : 385-1188

Herpes Simplex Virus Tyrosine Kinase PolyA signal : 1189-1249

FRT : 1250-1310

Linker sequences : 1311-1340



Fig. 17

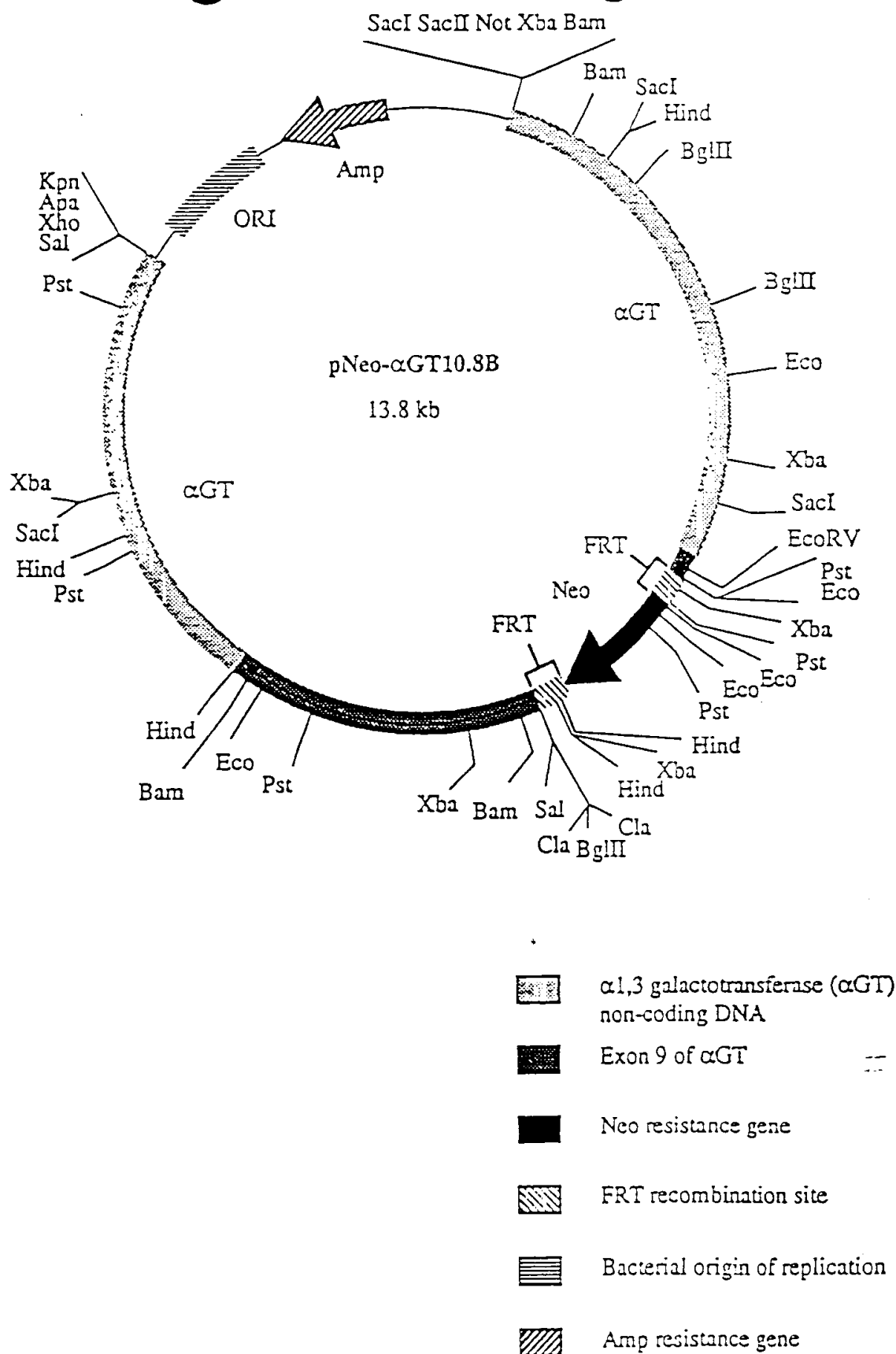
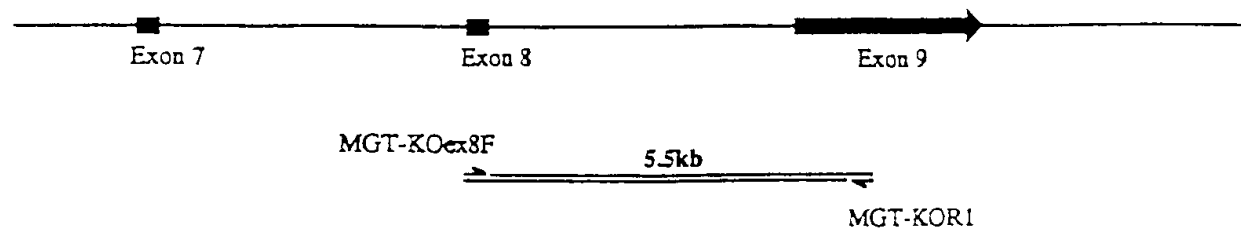


Fig. 17

Uninterrupted gene



Targeted gene

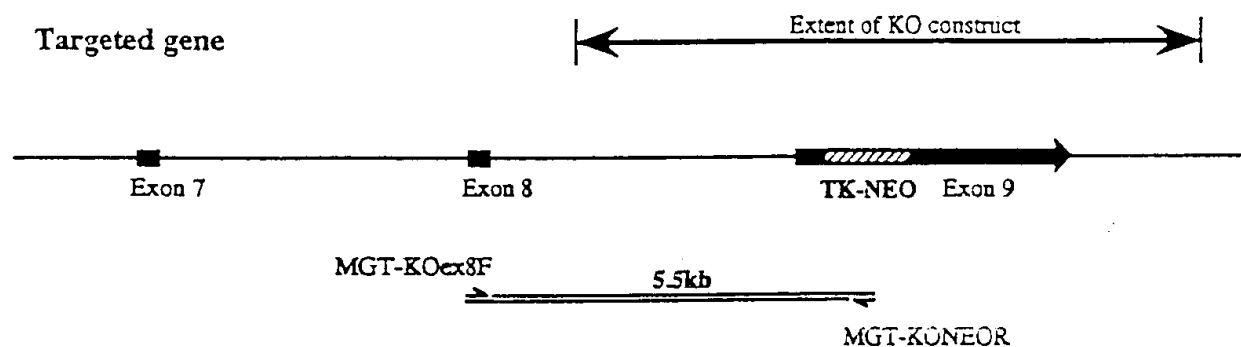
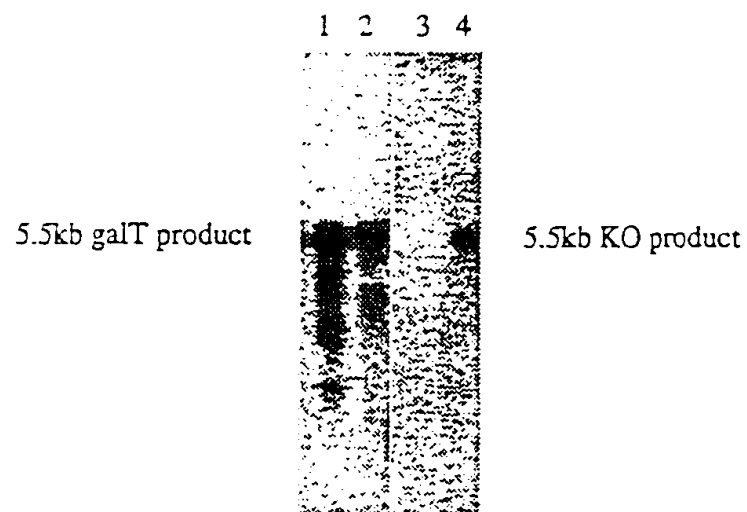


Fig. 18



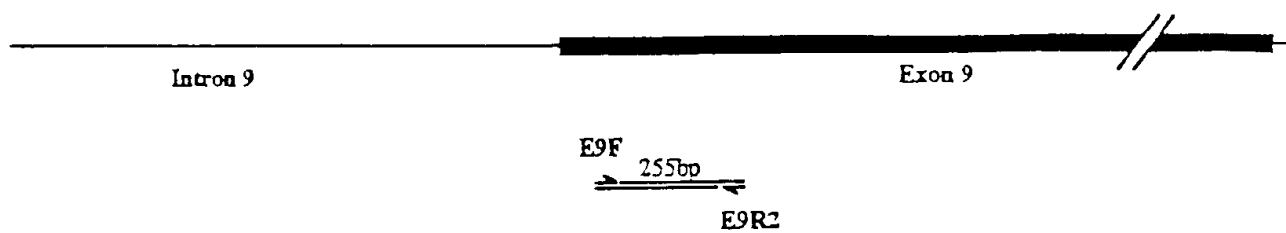
Fig.



1. CBAC template; wild type primers
2. 7C2 template; wild type primers
3. CBAC template; KO primers
4. 7C2 template; KO primers

Fig. 21

Uninterrupted gene



Targeted gene

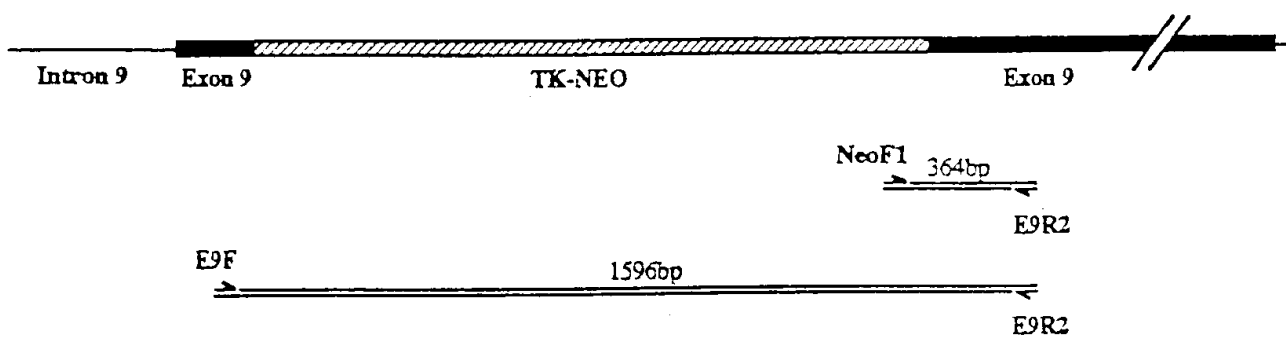


Fig. 22

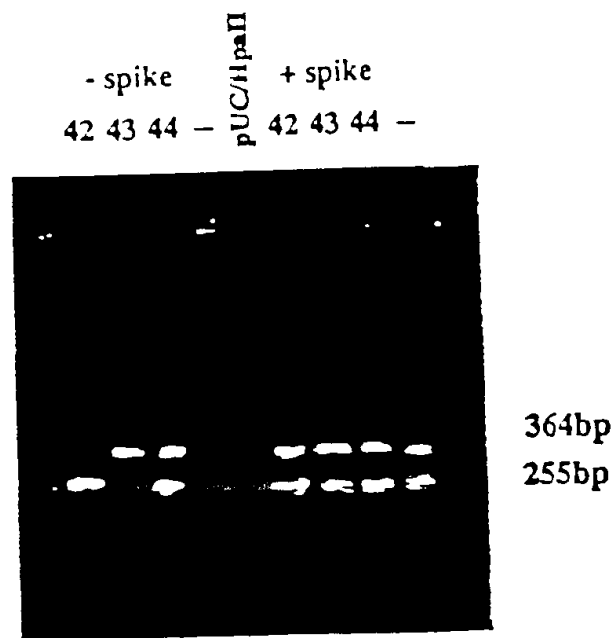
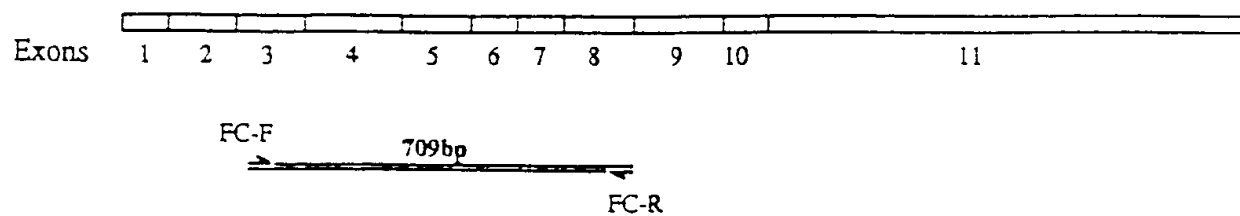
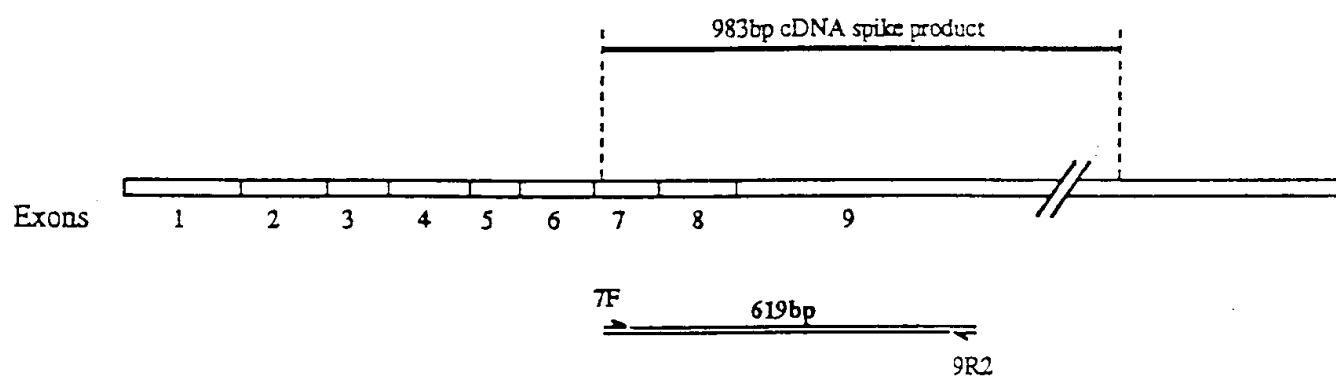


Fig. 23

Primer binding sites within mouse ferrochelatase cDNA

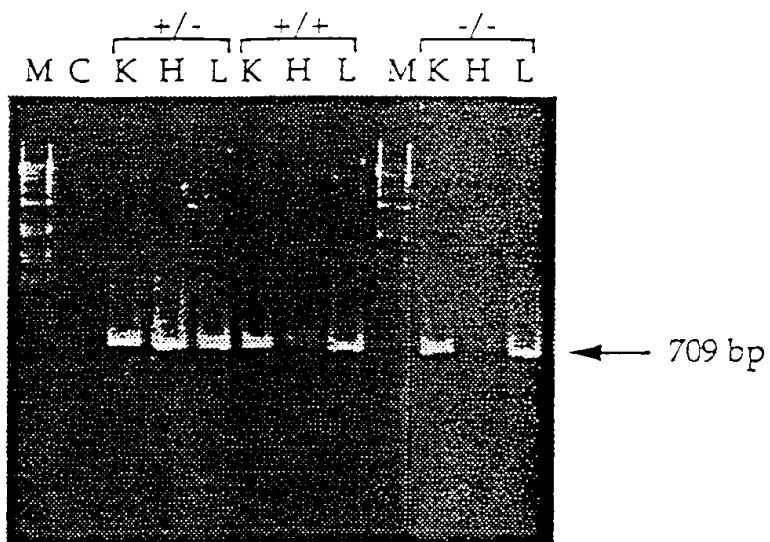


Primer binding sites within mouse  $\alpha$ -1,3-GalT cDNA

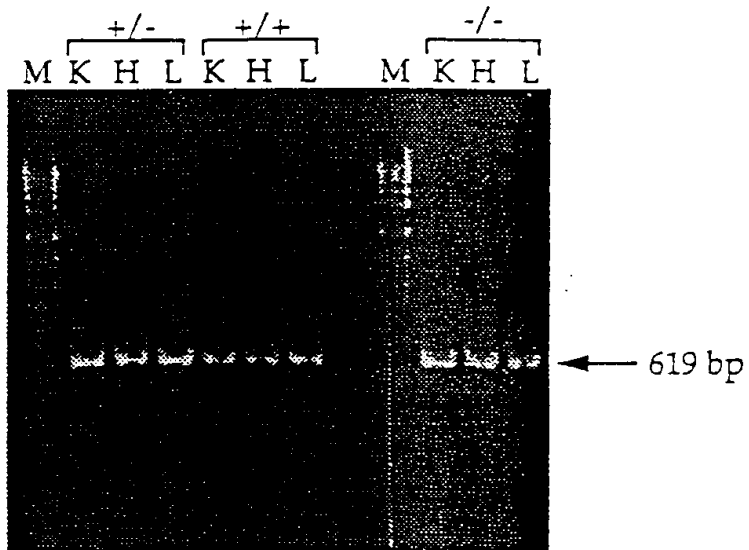


i) Ferrochelatase, FC-F/R

M, Marker SPP-I  
C, MQW control  
K, KIDNEY  
H, HEART  
L, LIVER



ii)  $\alpha$ -1,3-GT cDNA spike  
+ 7F/9R2 primers



iii)  $\alpha$ -1,3-GT 7F/9R2 primers

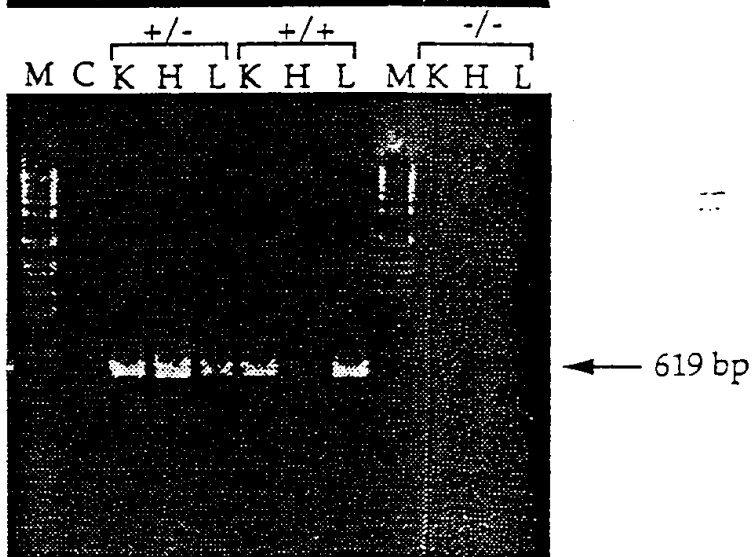
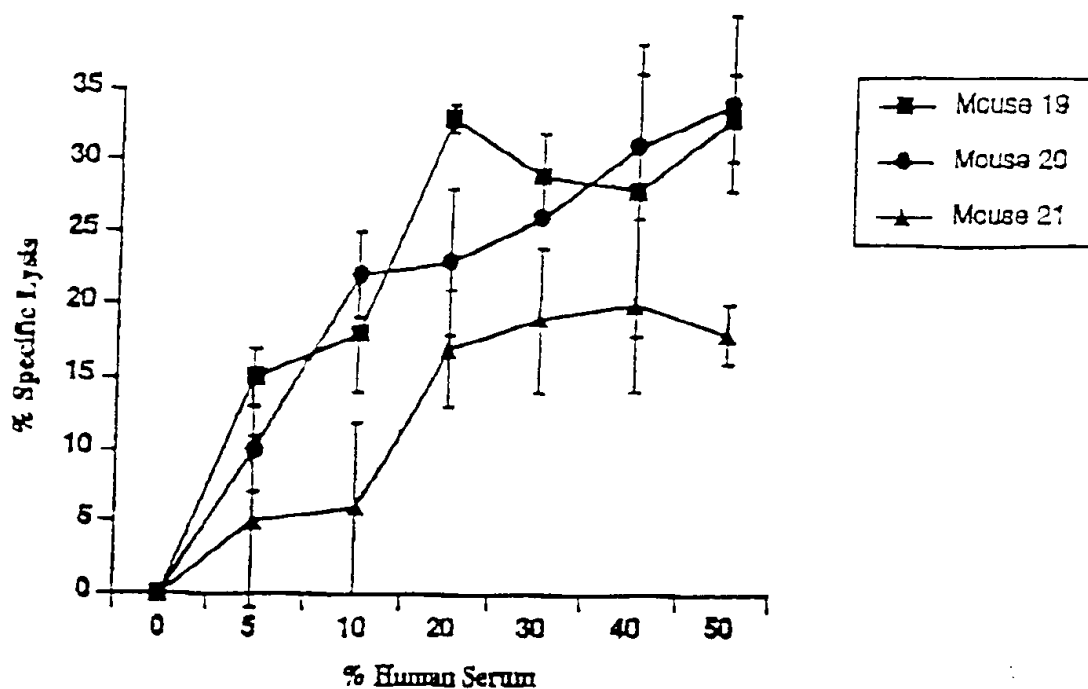




Fig. 25



Mouse 19: Wild type; Mouse 20: Heterozygote Gal KO; Mouse 21:  
Homozygous Gal KO

Fig. 26

T-LIF SEQUENCE - Murine

CTGACACCTTTGCTTTCTCTGCGTGTCGCGCTGCGACCTTTCCCCACCCC  
GGCCTCTTTCTGCTTGCACCACTTCCTCTCATTCCAAAGGATTGTGCCCTTA  
CTGCTGCTGGTTCTGCACTGGAAACACGGGGCAGGGAGCCCTCTTCCCATCAC  
CCCTGTAAATGCCACCTGTGCCATACGCCACCCATGCCACGGCAACCTC

Met	Asn	Gln	Ile	Lys	Asn	Gln	Leu	Ala	Gln	Leu	Asn	Gly	
ATG	AAC	CAG	ATC	AAG	AAT	CAA	CTG	GCA	CAG	CTC	AAT	GGC	
Ser	Ala	Asn	Ala	Leu	Phe	Ile	Ser	Tyr	Tyr	Thr	Ala	Gln	Gly
AGC	GCC	AAT	GCT	CTC	TTC	ATT	TCC	TAT	TAC	ACA	GCT	CAA	GGX
Glu	Pro	Phe	Pro	Asn	Asn	Val	Glu	Lys	Leu	Cys	Ala	Pro	Asn
GAG	CCG	TTT	CCC	AAC	AAC	GTG	GAA	AAG	CTA	TGT	GCG	CCT	AAC
Met	Thr	Asp	Phe	Pro	Ser	Phe	His	Gly	Asn	Gly	Thr	Glu	Lys
ATG	ACA	GAC	TTC	CCA	TCT	TTC	CAT	GGC	AAC	GGG	ACA	GAG	AAG
Thr	Lys	Leu	Val	Glu	Leu	Tyr	Arg	Met	Val	Ala	Tyr	Leu	Ser
ACC	AAG	TTG	GTG	GAG	CTG	TAT	CGG	ATG	GTC	GCA	TAC	CTG	AGC
Ala	Ser	Leu	Thr	Asn	Ile	Thr	Arg	Asp	Gln	Lys	Val	Leu	Asn
GCC	TCC	CTG	ACC	AAT	ATC	ACC	CGG	GAC	CAG	AAG	GTC	CTG	AAC
Pro	Thr	Ala	Val	Ser	Leu	Gln	Val	Lys	Leu	Asn	Ala	Thr	Ile
CCC	ACT	GCC	GTG	AGC	CTC	CAG	GTC	AAG	CTC	AAT	GCT	ACT	ATA
Asp	Val	Met	Arg	Gly	Leu	Leu	Ser	Asn	Val	Leu	Cys	Arg	Leu
GAC	GTC	ATG	AGG	GGC	CTC	CTC	AGC	AAT	GTG	CTT	TGC	CGT	CTG
Cys	Asn	Lys	Tyr	Arg	Val	Gly	His	Val	Asp	Val	Pro	Pro	Val
TGC	AAC	AAG	TAC	CGT	GTG	GGC	CAC	GTG	GAT	GTG	CCA	CCT	GTC
Pro	Asp	His	Ser	Asp	Lys	Glu	Ala	Phe	Gln	Arg	Lys	Lys	Leu
CCC	GAC	CAC	TCT	GAC	AAA	GAA	GCC	TTC	CAA	AGG	AAA	AAG	TTG
Gly	Cys	Gln	Leu	Leu	Gly	Thr	Tyr	Lys	Gln	Val	Ile	Ser	Val
GGT	TGC	CAG	CTT	CTG	GGG	ACA	TAC	AAG	CAA	GTC	ATA	AGT	GTG
Val	Val	Gln	Ala	Phe	***								
GTG	GTC	CAG	GCC	TTC	TAG	AGAGGAGGTCTTGAATGTACCATGGACTG...							

Fig. 27

# HUMAN T-LIF SEQUENCE

GACCTTTTGC CTTTTCTCTC TCCTGGTGCA CCATTTCCTC TCCCTCCCTG	50
AGCCGGAGTT GTGCCCCCTGC TGTTGGTTCT GCACTGGAAA CATGGGGCGG	100
GGAGCCCCCT CCCCATCACC CCTGTCAACG CCACCTGTGC CATAAGCCAC	150
CCATGTCACA ACAACCTC ATG AAC CAG ATC	182
Met Asn Gln Ile	
AGG AGC CAA CTG GCA CAG CTC AAT GGC AGT GCC AAT GCC CTC	227
Arg Ser Gln Leu Ala Gln Leu Asn Gly Ser Ala Asn Ala Leu	
5 10 15	
TTT ATT CTC TAT TAC ACA GCC CAG GGG GAG CCG TTC CCC AAC	272
Phe Ile Leu Tyr Tyr Thr Ala Gln Gly Glu Pro Phe Pro Asn	
20 25 30	
AAC CTG GAC AAG CTA TGT GGC CCC AAC GTG ACG GAC TTC CCG	317
Asn Leu Asp Lys Leu Cys Gly Pro Asn Val Thr Asp Phe Pro	
35 40 45	
CCC TTC CAC GCC AAC GGC ACG GAG AAG GCC AAG CTG GTG GAG	362
Pro Phe His Ala Asn Gly Thr Glu Lys Ala Lys Leu Val Glu	
50 55 60	
CTG TAC CGC ATA GTC GTG TAC CTT GGC ACC TCC CTG GGC AAC	407
Leu Tyr Arg Ile Val Val Tyr Leu Gly Thr Ser Leu Gly Asn	
65 70	
ATC ACC CGG GAC CAG AAG ATC CTC AAC CCC AGT GCC CTC AGC	452
Ile Thr Arg Asp Gln Lys Ile Leu Asn Pro Ser Ala Leu Ser	
75 80 85	
CTC CAC AGC AAG CTC AAC GCC ACC GCC GAC ATC CTG CGA GGC	497
Leu His Ser Lys Leu Asn Ala Thr Ala Asp Ile Leu Arg Gly	
90 95 100	
CTC CTT AGC AAC GTG CTG TGC CGC CTG TGC AGC AAG TAC CAC	542
Leu Leu Ser Asn Val Leu Cys Arg Leu Cys Ser Lys Tyr His	
105 110 115	
GTG GGC CAT GTG GAC GTG ACC TAC GGC CCT GAC ACC TCG GGT	587
Val Gly His Val Asp Val Thr Tyr Gly Pro Asp Thr Ser Gly	
120 125 130	
AAG GAT GTC TTC CAG AAG AAG AAG CTG GGC TGT CAA CTC CTG	632
Lys Asp Val Phe Gln Lys Lys Lys Leu Gly Cys Gln Leu Leu	

Fig. 27 (cont.) 27-2

	135	140	
GGG AAG TAT AAG CAG ATC ATC GCC GTG TTG GCC CAG GCC TTC			677
Gly Lys Tyr Lys Gln Ile Ile Ala Val Leu Ala Gln Ala Phe			
145	150	155	
TAG CAGGAGGTCT			722
***			

Fig. 28

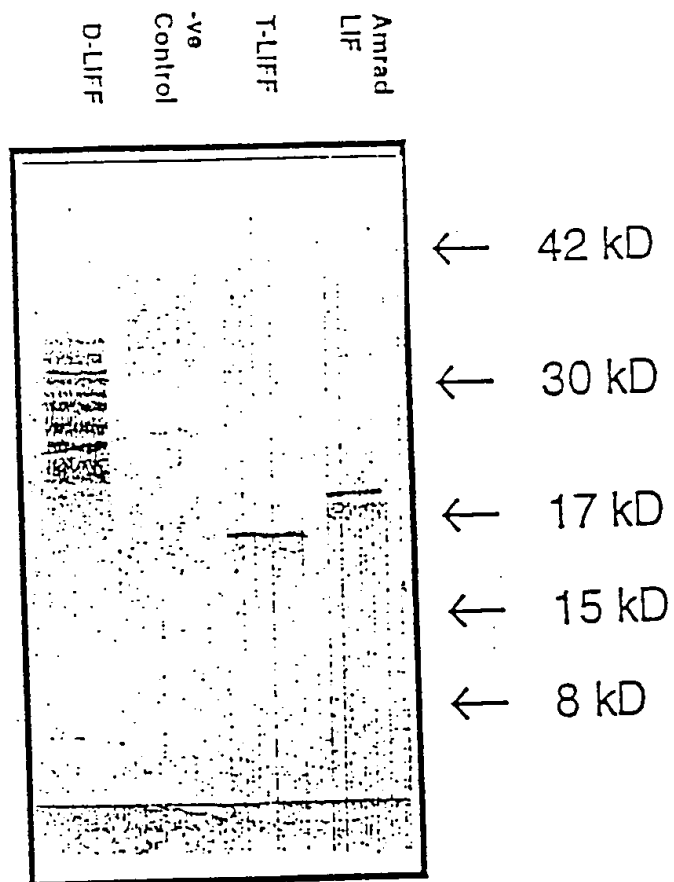
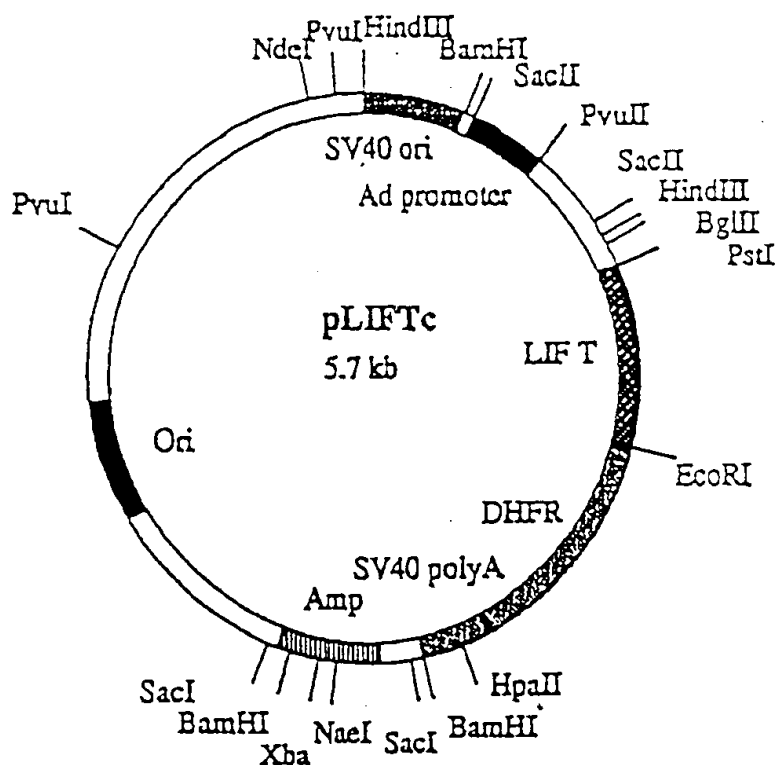


Fig. 29

(30)









-  SV40 origin of replication
-  Adenovirus promoter
-  LIF T coding region
-  Dihydrofolate reductase 3' end
-  Ampicillin resistance gene
-  Bacterial origin of replication

Fig. 30

